Draft Guidance for FDA Staff

Draft Compliance Program Guidance Manual: Inspection of Medical Devices

Draft Guidance – Not for Implementation

This guidance document is being distributed for comment purposes only.
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Level 1 Draft Guidance

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

Division of Program Operations
Office of Compliance

Preface

Public Comment:

Comments and suggestions regarding this draft document should be submitted by [date 90 days from release date] to Docket No. [99N-fill in], Dockets Management Branch, Division of Management Systems and Policy, Office of Human Resources and Management Services, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD 20852.

Additional Copies:

World Wide Web/CDRH home page at http://www.fda.gov/cdrh/ochome.html or CDRH Facts on Demand at 1-800-899-0381 or 301-827-0111, specify number 1702 when prompted for the document shelf number.

SUBJECT:	IMPLEMENTATION DATE
INSPECTION OF MEDICAL DEVICE MANUFACTURERS	Upon Receipt of Final Document
	COMPLETION DATE

DATA REPORTING

PRODUCT CODES	PRODUCT/ASSIGNMENT CODES
73-91	82845A 42830L -- All Level 1 (Abbreviated) Inspections 82845B 42830C -- All Level 2 (Baseline) Inspections 82845C -- All Level 3 (Compliance Follow-up) Inspections 82845G -- All For Cause Inspections 82845S -- Report Time spent on Assessment of Firm's Sterilization processes 81011 --Report Time spent on Assessment of Firm's MDR Practices 81845T --Report Time spent on Assessment of Firm's Tracking Practices 81845R -- Report Time spent on Assessment of Firm's Corrections and Removals Practices

Field Reporting Requirements

483s: A copy of all FDA-483s and the corresponding coversheet with endorsement should be sent to HFZ-306 for entry into the national 483 database.

EIRs: All EIRs resulting in a Warning Letter or a Post-Inspectional Notification Letter based on the firm's response to a violative inspection should be sent to CDRH, HFZ-306. All recommendations for administrative/regulatory action should include the EIR, FDA-483, and exhibits. The recommendations should be sent to HFZ-306.

Warning Letters: A copy of all Warning Letters should be sent to HFZ-306 and HFC-210**.**

Comment. If the district wishes to obtain comment from CDRH for any EIR, the district should attach a cover memorandum to the EIR outlining the issues to be considered by the Office of Compliance (OC). This policy does not relieve the district from COMSTAT reporting requirements.

NOTE: Design Control and Sterilization checklists are no longer needed.

This guidance document represents the agency's current thinking on the enforcement of the Quality System/Good Manufacturing Practices (QS/GMP), Medical Device Reporting (MDR), Medical Device Tracking, Corrections and Removals (CAR), and the Registration and Listing regulations. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

PAC Guidance

PROGRAM	PACs
Quality System	Level 1 (82845A)
	Level 2 (82845B)
	Level 3 (82845C)
For Cause	82845G
MDR	81011
Tracking	81845T
CAR	81845R
Sterilization Inspections*	82845S

* These inspections are sub-inspections of the Quality System Program. When conducting sterilization review as part of the Production and Process Controls subsystem, report **only** the time spent reviewing the sterilization process during the Quality System inspection, if covered. The sterilization time should be reported under PAC 828345S. Also, report PACs, 81011, 81845T and 81845R, as applicable.

The above PAC Guidance is provided for investigator reference only. It's sole purpose is as a memory jogger, to assist in the PAC reporting activity.

TOPIC	COMPLIANCE PROGRAM PART NUMBER AND PAGE LOCATION							
	CS	I	II	III	IV	V	VI	ATTACHMENT
Administrative/Regulatory Action (Enforcement Action)	1	1	1	3, 5-7, 12		1-16	9, 12	C 1-7
Attachment Titles							6-7	
Audits				5		7-9, 14		C 1, 3-4, 6 F 3
Case Experts (Case Officers)						9, 11	11-12	
Class I Devices			4-6	6, 11			6	A 1-14
• Class I Exempt Devices			5-6	11			6	A 1-14
Class II/III Devices			3-6	11				B 8, 11 C 2, 4
Complaints (Complaint Files)		2	5-6	5, 8		13		C 1, 3 E 4-5, 7
COMSTAT	1		2	10-11			1, 8	
Concurrence & Consulting Required	1		1	1, 7, 13		1, 3, 7, 9-15		
Consultant				9		8-9		C 4-7 E 5
Contacts (Inform)			7	6-7, 11-12	1	9, 11-12, 15-16	3, 7-12	D 2 E 1, 5, 8-10 F 3
Corrections and Removals (CAR)	1-2	1, 3	1	1, 5-6		14-15	7	G 1-5
Critical/Significant Risk Devices/High Risk Devices			3-7	10		3	2, 7	B 1-18 B-1 1-3
Design Control ***(see Subsystems: Design Controls)***								

TOPIC	COMPLIANCE PROGRAM PART NUMBER AND PAGE LOCATION							
	CS	I	II	III	IV	V	VI	ATTACHMENT
Distributor		2-3	1			9		E 1, F 1-3 G 2-3
Electronic Records and Electronic Signatures						15-16	11	
Exports				11				
FDA Modernization Act		2						
Food, Drug & Cosmetic Act (FD&C Act or the Act)				8, 10-11		3, 5, 8, 10	1	C 1-4 E 8 G1
Guide to Inspections of Quality Systems (QSIT Guide)		2	2-3, 5-6	1-3, 5-9, 11, 13		1, 3-4	1	
Importer or Imports		1-3	1	11				F 1 G 1-3
In Vitro Diagnostic Devices (IVDs)		2			1		2	
Inspectional Observations Form FDA-483	1		6	4, 9, 13		3, 10-16		C 2, 4
Inspection Priorities			3-6	4-6				
Inspectional Procedures	2			4-11		3, 13		
Inspectional Strategy ***(also known as Quality System Inspection Technique [QSIT])***	1-2	1	2-6	1-6, 8, 11		7		
INSPECTION TYPES: Abbreviated EI	1		3	1-2, 6, 12				
Baseline (Comprehensive) EI	1		3, 5	1-4				
Follow-up EI	1		3-4, 6	1, 3, 7		5, 7-9		C 5
For Cause EI	2	1-2		8				

TOPIC	COMPLIANCE PROGRAM PART NUMBER AND PAGE LOCATION							
	CS	I	II	III	IV	V	VI	ATTACHMENT
Foreign EI				7				
Initial EI			5	4				
Level 1	1-2		3, 5	1-2, 4-6		3		
Level 2	1-2		3, 5	1-6		3		
Level 3	1-2		3, 6	1, 3-4, 6		4, 7		
Pre-Approval EI			2					
Routine EI			3, 5	1-2, 6, 12				
Medical Device Reporting (MDR)	1-2	1-2	1, 4, 6	1, 5-6, 12		12-13	2, 3, 7, 9	C 1-4 E 1-10 G 1
Medical Device Tracking	1-2	1-2	1	12		13-14	2, 7	F 1-4
OC Organizational Chart						9, 11	13	
Packaging (seal)				6-7	1-3	5	2, 4-6	C 1, 3
Post-Inspectional Notification Letter	1		6	11				
Premarket Notification 510(k)			3-4	8, 13				B 8 C 4, 6 D 1
Premarket Approval (PMA)			4	8		10		B 6, 9-10 C 4, 6 D 1
Pre-Notification			6					
Product Assignment Codes (PAC)	1-2		5-6	1, 10				
Profile Classes			2, 4-5	10-11				
Profile Data Sheet			4-5	11		7-8		

TOPIC	COMPLIANCE PROGRAM PART NUMBER AND PAGE LOCATION							
	CS	I	II	III	IV	V	VI	ATTACHMENT
Quality Assurance (QA)	1	1	6	8		4, 7-8		C 1-4 F 3
Quality System Regulation or Requirements	2	1	1, 5-6	1-6, 10-13		1-10, 15	1-2, 9-10	B 2 C 1-3
Radiation Emitting Device				10			4, 5	
Recalls	2	2	4			3, 6-7, 9, 14		D 2 G 2, 4
References (Publications)							1-6	G 4
Registration and Listing	2	1, 3	1-2, 5-6	1, 6, 12, 13				B 17
Repacker/Relabeler			3-4	12		9		
Reporting Requirements & Info.	1-2	2	6-7	12-13		3-11		E 1-8 F 1-4 G 1-3
Samples				6-7, 10-11	1-3	3-4, 10-12		
Sampling Records						3-4		
Situation I			3-4	3-4, 11		1-4, 7, 9, 11-13, 15		
Situation II				2, 4		3		
Specification Developers			3-4					
Sterilization/sterility	1-2	1	2, 4, 7	5-10	1-3	4-5	3-6, 10	B 17
SUBSYSTEMS: Corrective and Preventive Actions (CAPA)		1-2	4-5	1-8		1-2		D 2
Design Controls	2	1	2	1-5, 8-9		2, 6, 8	2	D 1-2
• Design Control Records				8			7	D 1-2
Production and Process Controls (P&PC)	2	1		1-6, 9, 11		2		

TOPIC	COMPLIANCE PROGRAM PART NUMBER AND PAGE LOCATION							
	CS	I	II	III	IV	V	VI	ATTACHMENT
Management Controls		1		1-5		1-2		
Facilities and Equipment Controls		1		1		2		C 1, 3
Materials Controls		1		1		2		
Documents/Records/Change Controls		1		1		2		D 2
Surgical Implant or Sustaining Life Devices		2	5	10			6	B 1-26 B-1 1 E 8
Tracking ***(see Medical Device Tracking)***								
Web Sites			3			3	3, 4, 12	E 9-10
Warning Letters	1		6	3, 6		3-16	7	C 1-7
• Model Warning Letters						6-8	7	C 1-7

PART I

BACKGROUND

- **This compliance program provides guidance to the FDA field and center staffs for the inspections and administrative/enforcement activities related to the Quality System/Good Manufacturing Practices (QS/GMP) regulation (21 CFR Part 820), the Medical Device Reporting (MDR) regulation (21 CFR Part 803), the Medical Device Tracking regulation (21 CFR Part 821), the Corrections and Removals regulation (21 CFR Part 806), and the Registration and Listing regulation (21 CFR Part 807).**

  This compliance program encompasses five regulations for inspecting medical device firms. Under the QS/GMP regulation, manufacturers are expected to control their products from birth to death, meaning from design stage through post-market surveillance. Their manufacturing processes, such as sterilization, are required to be under control. The MDR, Tracking, and Corrections and Removals regulations cover the activities with which manufacturers and initial importers are involved after the devices are distributed. This compliance program provides specific guidance for each. It also suggests some coverage for Registration & Listing.

A. THE QUALITY SYSTEM (QS/GMP) REGULATION

This compliance program provides a strategy designed to produce more efficient, focused and more harmonized (with the international community) QS/GMP inspections, and address issues of non-compliance. This new inspectional strategy is designed to compensate, in part, for the increasing strain on field resources while, at the same time, providing for regulatory action when required. A new enforcement criteria is provided in Part V, which ties to the new inspection approach.

This strategy is called the Quality System Inspections Technique (QSIT). QSIT is based on a "top-down" inspection of a manufacturer's quality system, using the seven subsystems of the Quality System regulation. The seven subsystems are: Corrective and Preventive Actions (CAPA), Design Controls, Production and Process Controls (P&PC), Management Controls, Facilities and Equipment Controls, Materials Controls, and Documents/Records/Change Controls.

The "top-down" inspectional approach begins looking at a firm's "systems" for addressing quality problems, as opposed to a "bottom-up" approach, which starts by looking at one or more problems that may point to a failure in the quality system. The strategy, outlined in this program, continues to place emphasis on manufacturers' responsibility to monitor their compliance with QS/GMP requirements, and to make appropriate and timely corrections of problems in their design, manufacturing, and quality assurance systems.

Important Note: "**For Cause**" inspections can still be conducted as the need arises. These inspections are generally more in-depth than the QSIT inspections. (See Part III, page 8, for additional information regarding For Cause inspections) These inspections should be directed toward finding the quality problems, tracing the root causes and assuring the appropriate corrective and preventative actions are initiated. For Cause inspections are usually initiated as a result of CDRH, ORA headquarters, Regional or District directives. They are most often initiated as a result of a serious health risk, which was brought to the attention of FDA. Immediate investigations/inspections are needed in these cases. These inspections can be conducted using the Guide to Inspections of Quality Systems, also called the QSIT Guide. However, more in-depth investigations are often needed in the CAPA area. NOTE: See Part III for additional information regarding the QSIT Guide.

B. THE MDR REGULATION

The first Medical Device Reporting (MDR) regulation became final on December 13, 1984. As a result of changes mandated by the Safe Medical Devices Act (SMDA) of 1990, and the Medical Device Amendments of 1992, the 1984 MDR regulation was revised and published on 12/11/95. The FDA Modernization Act of 1997 made additional changes to MDR and a revised MDR Regulation was proposed in May 1998. The agency is currently evaluating comments on the proposed changes to the regulation. A final MDR regulation will be published in the Summer or Fall of 1999. The latest version of MDR will include reporting requirements for both manufacturers and importers and will revoke 21 CFR Part 804. However, until a final MDR regulation is published, importers are still subject to the MDR reporting requirements in 21 CFR Part 804. Please note that MDR reporting for medical device distributors (except importers) was revoked by the FDA Modernization Act of 1997. Distributors are, however, still required to maintain complaint files.

21 CFR Part 803 requires manufacturers of medical devices, including in vitro diagnostic devices, to report to FDA whenever the manufacturer or importer receives or otherwise becomes aware of information that reasonably suggests that one of its marketed devices:

1) may have caused or contributed to a death or serious injury or,
2) has malfunctioned and that the device or any other device marketed by the manufacturer or Importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

NOTE: Importers (initial distributors) of medical devices will be subject to 21 CFR Part 803 when the MDR regulation is finalized.

C. THE MEDICAL DEVICE TRACKING REGULATION

The Tracking regulation requires certain manufacturers to implement a method of tracking for permanently implanted or life sustaining/supporting devices used outside a device user facility, the failure of which would be reasonably likely to have serious adverse health consequences. This regulation is intended to ensure that in the event of a recall or safety alert a tracked device can be traced from the device manufacturing facility to the patient.

D. THE CORRECTIONS AND REMOVAL REGULATION

The Corrections and Removal (CAR) regulation requires manufacturers, importers, and distributors to report promptly to FDA corrections or removals of devices undertaken to reduce risk to health.

E. THE REGISTRATION AND LISTING REGULATION

The Registration and Listing regulation requires manufacturers and own label distributors to register

and list their devices; and initial importers to register.

PART II

IMPLEMENTATION

FDA staff should not deviate from this guidance without appropriate justification and supervisory concurrence.

A. OBJECTIVES

QUALITY SYSTEM/GMP REGULATION

1. To identify domestic and foreign manufacturers who are not in compliance with the Quality System regulation. To bring such manufacturers into compliance through voluntary, administrative or regulatory means, as appropriate.

MEDICAL DEVICE REPORTING REGULATION

2. To identify manufacturers and importers who are not in compliance with the Medical Device Reporting (MDR) regulation. To bring such firms into compliance through voluntary, administrative or regulatory means, as appropriate.

MEDICAL DEVICE TRACKING REGULATION

3. To identify manufacturers and importers who are not in compliance with the Medical Device Tracking regulation. To bring such firms into compliance through voluntary, administrative or regulatory means, as appropriate.

CORRECTIONS AND REMOVALS REGULATION

4. To determine if manufacturers and distributors are making good faith efforts to comply with the Corrections and Removals (CAR) regulation. To bring such firms into compliance through voluntary, administrative or regulatory means, as appropriate.

REGISTRATION AND LISTING REGULATION

5. To identify firms who are not in compliance with the Registration and Listing regulation. To bring such firms into compliance through voluntary, administrative or regulatory means, as appropriate.

B. PROGRAM MANAGEMENT INSTRUCTIONS

1. The following guidelines are suggested for implementing this compliance program

a. This compliance program is to be used to conduct Compliance Status Information System (COMSTAT) inspections of devices when directed by HFC-240. This is in accordance with the current COMSTAT Manual and to obtain data for COMSTAT profiles and/or updates during regularly scheduled QS/GMP inspections.

b. Many large firms have several manufacturing facilities located in more then one district. These firms often have a research and development (R&D) center or corporate design facility which services several manufacturing facilities. Upon completing an inspection of an R&D center or corporate design facility, districts should send copies of the inspection report to the home districts of the firms' manufacturing facilities. Unless additional information must be obtained from the manufacturing facility, the home district of the manufacturing facility will not need to conduct a routine design control assessment if an inspection of the R&D center or corporate design facility was conducted within the previous two years. If an inspection of the R&D center or corporate design facility has not been conducted within the previous two years, the home district of the manufacturing facility should issue an assignment to the home district of the R&D center or corporate design facility requesting a design control inspection. The above guidance is NOT applicable to Pre-Approval inspections.

Many large firms also have design facilities located in sites that were previously not required to register. Such establishments should be advised of their registration obligation by the district and assigned a Central File Number.

c. Sterilization of medical devices, a process formerly covered under separate circulars (7382.830A and 7382.830B) to the QS/GMP compliance program is no longer covered under separate circulars. Sterilization is now covered as a part of the QSIT inspection under this compliance program. Guidance provided in the QSIT Guide is to be followed in inspecting sterilization processes for the following types of facilities:

- device manufacturers that sterilize their own product;
- device manufacturers that use contract sterilizers; and,
- contract sterilizers.

d. Medical Devices related to AIDS diagnosis, blood banking and/or human blood processing will be inspected under this compliance program. For guidance, see the Intercenter Agreement between the Center for Biologics Evaluation and Research and the Center for Devices and Radiological Health, dated October 31, 1991. The Biologics and Devices Intercenter Agreement can be found at the following web site: http://www.fda.gov/oc/ombudsman/bio-dev.htm

2. Scheduling Inspections of Medical Device Manufacturers

a. Priorities for QS/GMP Inspections

The Field Workplan for Inspection of Medical Device Manufacturers provides for inspection of half of each inventory of high risk devices and 40 percent of manufacturers of Class III devices. Most of the districts also have resources planned for inspections of Class II and I devices.

Important Note: Quality System/GMP inspections should be conducted using the Quality System Inspection Technique (QSIT). The guidance for "how to" perform the inspections are provided in the Guide to Inspections of Quality Systems, also called the QSIT Guide. The QSIT tool can be scaled to meet the needs of each particular inspection. QSIT consists of three inspection levels. Level 1 inspections are considered Abbreviated Inspections. Level 2 inspections are considered Baseline (Comprehensive) Inspections. Level 3 inspections are considered Compliance Follow-up Inspections. See Part III for additional information concerning the QSIT Guide, specifically the inspection levels.

During FY 1999 and 2000, district management should schedule inspections of device establishments according to the following priorities:

Priority A Manufacturers of High Risk and Class III Devices That Have Not Been Inspected Within the Last Year. Please schedule inspections of establishments that actually manufacture devices before those that are only specification developers or repackers/relabelers. Specification developers that are part of firms that actually manufacturer a device(s) should be scheduled for concurrent inspections whenever possible.

1. Manufacturers that have never been inspected.
2. OAI follow-up inspections.
3. Manufacturers that received their last inspection more than two years ago and manufacturers for which there is an outstanding routine priority assignment.
4. Any other manufacturer of high risk or Class III device.
5. Establishments that are only specification developers or repackers/relabelers.

Priority B Manufacturers of Class II and I Devices Please schedule inspections of establishments that actually manufacture devices before those that are independent specification developers or repackers/relabelers. Specification developers that are part of firms that actually manufacturer a device(s) should be scheduled for concurrent inspections whenever possible.

1. Manufacturers of Class II devices that have never been inspected.
2. OAI follow-up inspections of manufacturers of Class II or I devices.
3. Manufacturers of Class II or I devices that have conducted more than two recalls in the last 12 months.
4. Manufacturers of Class II or I devices that have recently experienced an increase in MDR reports.

5. Manufacturers of Class II devices that have received 510(k)s within the last two years.
6. Any other manufacturers of Class II devices.
7. Establishments that are only Class II specification developers or repackers/relabelers.
8. Manufacturers of Class I devices that have never been inspected.
9. Manufacturers of Class I sterile devices.
10. Any other manufacturers of Class I devices.

Note: Inspections of manufacturers of devices with a pending PMA approval will be assigned under the PMA Compliance Program (7383.001).

- Inspectional assignments that support the previously referenced program should be conducted using a **Level 2** QSIT inspection as well as specific guidance in the program and/or the assignment. The district may count the inspection as a QS/GMP inspection when the inspection covers all profile classes (except those associated exclusively with certain Class I devices). NOTE: If all profile classes are not directly covered during an inspection, but are covered indirectly under CAPA, then all profile classes the firm is involved with can be listed on the Profile Data Sheet and thus the district may count the inspection as a QS/GMP inspection.

Note: Inspections of manufacturers that have submitted 510(k)s for preamendment Class III devices will be assigned under Compliance Program 7383.003. (See B.2.b. below for additional information relating to this program).

All other manufacturers should be inspected as resources permit. The primary goal of emphasizing inspection of the above device manufacturers is to change the scheduling of inspections from one that is purely based on the interval since the last inspection to one that also considers the health-hazard significance of the device. Conducting the inspection shortly after a 510(k) has received clearance will also allow an evaluation of manufacturers at the most critical stage of production. Because most manufacturing and design problems develop or become apparent within the first year of the device's life cycle, inspecting at this time should provide a better opportunity for identifying manufacturing and design problems. QS/GMP inspectional coverage will be focused on that segment of the industry that is actively bringing devices to market and thus presenting the most risk to the public.

b. QS/GMP Pre-Clearance Inspection Program for Class III 510(k) Pre-amendments Devices (CP 7383.003)

Inspectional assignments that support this program should be conducted using a **Level 2** QSIT inspection as well as specific guidance in the program and/or the assignment. The district may count the inspection as a QS/GMP inspection when the inspection covers all profile classes (except those associated exclusively with certain Class I devices). NOTE: If all profile classes are not directly covered during an inspection, but are covered indirectly under CAPA, then all profile classes the firm is involved with can be listed on the Profile Data Sheet and thus the district may

count the inspection as a QS/GMP inspection.

c. Initial Inspections

Newly registered and listed firms should receive a **Level 2** inspection per the QSIT Guide as soon as possible after manufacturing operations commence. Generally, firms that manufacture Class III devices and devices listed in Attachments B and B-1 should be inspected within 6 months and firms that manufacture all other Class II devices within 12 months. If the device(s) classification is not known in advance and cannot be determined otherwise, i.e., phone contact, catalog review, etc., the district should schedule the inspection and determine the appropriate inspectional approach after identifying the device(s). For guidance in determining if an establishment should be subject to the Quality System regulation, refer to Exhibit 590-A of the IOM.

If it cannot be determined that at least one device is Class II, III, or Non-QS/GMP exempt Class I, as discussed in section B.2.f. below, the district should review the firm's complaint handling practices, then terminate the inspection. The district should report the time against PAC 82R800 (District Initiated Assignment).

d. Routine Inspections

Ideally the goal is to conduct Baseline (Comprehensive) **Level 2** Quality System Inspection Technique (QSIT) inspections of all manufacturers of high risk devices as identified in Attachments B, B-1 and of 80 percent of the manufacturers of other Class III devices once every two years. After the first two years, the non-violative manufacturers should receive less intensive **Level 1** QSIT inspections with the result that resources would be available in subsequent years for more initial **Level 2** inspections of Class II and I device manufacturers.

e. Statutory Coverage List (formerly the Alert List)

Any registered firm that manufactures Class II or III devices and has not had a inspection during the previous 24 months will appear on the district's Statutory Coverage List (formerly the alert list).

The Statutory Coverage List (formerly the Alert List) will be based on the date of the last inspection (i.e., the last QS/GMP, inspection under PAC's 82830 L, C, or F, 83001, 83003, or 42830 C, or L) up to MM/DD/YY. NOTE: An actual date, which is dependent upon the effective date of this program, is unknown at this time. After the effective date of this compliance program the following PACs will also be eligible: 82845 A, B, C, or G.

f. Class I Device Manufacturers

All Class I devices, including those exempted from most of the Quality System regulation requirements, must comply with the complaint file requirements as well as the reporting requirements of the MDR regulation. Class I manufacturers should receive lowest inspectional priority unless addressed by a special assignment or a health

hazard is apparent. See Attachment A for those Class I devices that are exempt from most QS/GMP requirements.

g. Follow-up Inspections

A Warning Letter to a manufacturer alerts the manufacturer of its responsibility for reviewing all manufacturing and quality assurance systems. All follow-up inspections should be Level 3 QSIT inspections as explained in Part III.

Follow-up inspections conducted to determine if violations have been corrected should be reported against PAC 82845C.

3. Pre-notification of Inspections

Evaluation of the pilot phase of the Medical Device Industry Initiatives (MDII) for pre-notification of inspections, annotated FDA-483s and Post Inspectional Notification Letters identified benefits for both the industry and FDA. Consequently, the program has been made permanent. Refer to the Guide to Inspections of Quality Systems for specific guidance.

4. Resource Instructions

When possible, Electro-Optical Specialists should be used for inspection of laser devices.

Experienced investigators with specialized knowledge should conduct inspections of establishments that are manufacturing high-risk devices. Contact DEIO (HFC-133) should the need for expertise, not available in the Region, become apparent (Refer to FMD No. 142).

Inspections of sterilization processes should be performed only by those investigators who have the necessary training or experience to evaluate a sterilization process. Attendance at the Industrial Sterilization for Drugs and Medical Devices training course is highly recommended for investigators that perform inspections under this program.

PART III

INSPECTIONAL

FDA staff should not deviate from the guidance in this Part without appropriate justification and supervisory concurrence.

BACKGROUND

- **This program includes guidance for determining compliance with the Quality System/Good Manufacturing Practices (QS/GMP) regulation, Medical Device Reporting (MDR) regulation, Medical Device Tracking regulation, Corrections and Removals regulations, and the Registration and Listing regulation.**

A. OPERATIONS

1. Inspectional Strategy

   a. Quality System/GMP inspections should be conducted using the Quality System Inspection Technique (QSIT). Guidance for "how to" perform the inspections is provided in the Guide to Inspections of Quality Systems, also called the QSIT Guide. The QSIT tool can be scaled to meet the needs of each particular inspection. Using the QSIT TABLE, decide which type of inspection is being conducted, and cover the appropriate sections in the QSIT Guide.

QSIT TABLE

Inspection Level	Reason for Inspection	QSIT Subsystems Inspected
1	Abbreviated	CAPA plus one subsystem (PAC 82845A)
2	Baseline (Comprehensive)	The four major subsystems (PAC 82845B)
3	Compliance Follow-up	As directed by inspection guidance (PAC 82845C)

NOTE: Although the Quality System regulation has seven subsystems, the following four subsystems are considered major subsystems and are the basic foundation of a firm's quality system: Management Control, Design Control, Corrective and Preventive Actions (CAPA), and Production and Process Controls (P&PC). The three remaining subsystems (Facilities and Equipment Controls, Materials Controls and Document/Records/Change Controls) cut across a firm's quality system and can be evaluated while covering the four major subsystems.

LEVEL 1 – Inspections

Abbreviated Inspections are considered Level 1 inspections. Level 1 inspections can be done at the district's discretion on firms that passed a previous Baseline inspection

and those where the last inspection was classified VAI or NAI.

Note: All firms should have one Baseline (Comprehensive) inspection using the Level 2 QSIT approach. The Level 2 inspection is considered the Baseline for determining a firm's compliance with the quality system regulation. Under the workplan, a limited number of Level 1 inspections will be done on firms who have NOT had a prior Level 2 QSIT inspection. While it is not preferred to do Level 1 inspections without doing the Level 2 inspection prior, this will happen due to workplan statistics. These inspections should be done on firms who have had a thorough review of their quality system in the past five years.

Abbreviated inspections are considered Level 1 QSIT inspections. Level 1 inspections always must cover the CAPA subsystem plus one other subsystem, using the QSIT Guide.

Prior to deciding which subsystems to inspect (in addition to the CAPA subsystem) determine if there were:

- Changes in management control procedures
- Management control changes
- Changes in design control procedures
- Design changes
- Changes in production & process control procedures
- Production & process changes

Your findings from the above determination can assist in your decision of where to inspect in addition to the CAPA subsystem. Before choosing which subsystem to inspect as the "plus one", review the previous EIR(s) and determine which subsystems were covered. The "plus one" subsystems should be rotated, so that as many subsystems as possible are covered in the period between the Level 2, Baseline (Comprehensive) inspections. However, the determination listed above can also assist you in choosing which subsystem should be the "plus one".

LEVEL 2 – Inspections

Baseline (Comprehensive) Inspections are considered Level 2 inspections. The Level 2 inspection is considered the Baseline for determining a firm's compliance with the quality system regulation. For these inspections, cover all four major subsystems as explained in the QSIT Guide. All firms should have one Level 2 inspection to provide the agency with an overview of the firm's quality system. Once the Baseline is established, Level 1 inspections should be performed. However, as resources permit, these firms should get Level 2 inspections.

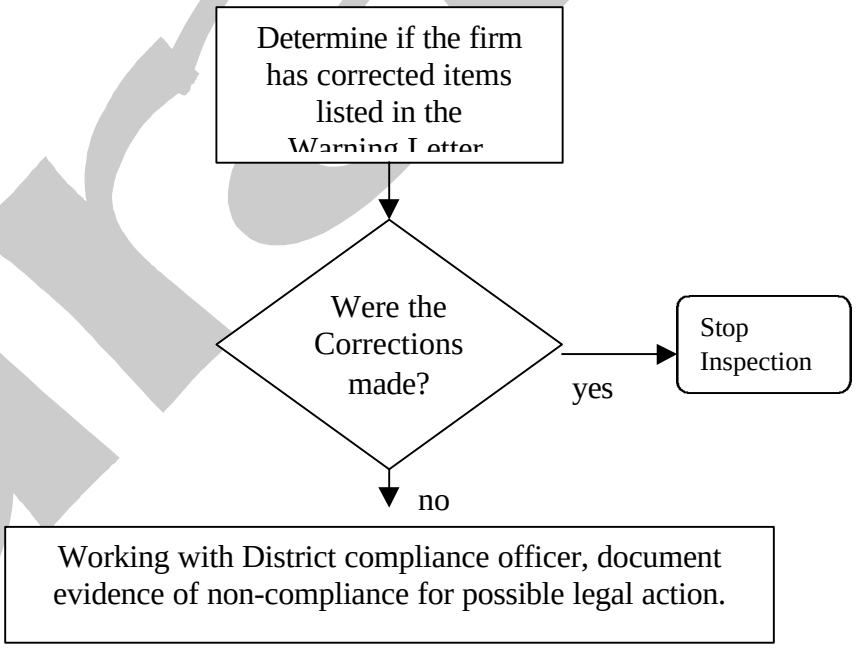
Note: As district resources permit, conduct a Baseline (Level 2) inspection every 6 years.

Note regarding Level 2 inspections: The QSIT approach, which evaluates all four major subsystems (management controls, design controls, corrective & preventative actions (CAPA), and production & process controls) is considered a complete review of the firm's entire quality system. Thus it is not necessary to inspect beyond the questions and inspectional guidance in the QSIT Guide unless you are asked to perform a Level 3 inspection.

LEVEL 3 – Inspections

Compliance Follow-up Inspections are considered Level 3 inspections. As mentioned in Part V of this compliance program, these Level 3 inspections are necessary AFTER a firm was found to have Situation I conditions under a previous Quality System/GMP inspection (the firm should have an OAI classification for the previous inspection). During Level 3 inspections you are expected to: (A) verify that adequate corrections have or have not been made to the quality system problems previously identified and (B) if the corrections were not made, verify that the violations continue to exist, and provide adequate evidence to support a possible regulatory action. Use the chart below to determine how far to go for the Level 3 inspection. You should also use the QSIT Guide for guidance, but work closely with the district compliance officer during Level 3 inspections to assure that you covered the areas at enough depth, documented the items appropriately, and collected sufficient evidence for regulatory action recommendation. See Part V, section A.5.b of this compliance program for additional guidance on these inspections.

Level 3 Inspections: Guide for choosing how far to go on compliance follow-up inspections.



b. Policy for Fatal Flaw situations. (See *Fatal Flaw statement* below)

Note regarding Fatal Flaw: It is important to establish a baseline that includes evaluations of CAPA, Design Controls, Production and Process Controls, and Management Controls subsystems. Therefore, during the QSIT Level 2, Baseline (Comprehensive) inspection at each manufacturer **do not** exercise the fatal flaw principle. The agency should evaluate the firm's entire quality system. Exercising the fatal flaw principle without evaluating their entire quality system at least once would not provide a complete analysis of the medical device firm's quality systems.

Decision for when to use "fatal flaw".

Last Inspection	Last Inspection was QSIT level	This Inspection is QSIT level	Use fatal flaw?
Firm was never inspected	-	2 *	No
NAI or VAI	2	1 or 2	Yes
NAI or VAI	1	1 ** or 2	Yes
OAI	1, 2, 3	3 ***	No

* Initial inspections should almost always be Level 2 QSIT inspections. Fatal flaw can not be used on initial inspections.
** Fatal flaw can only be used if a Level 2 QSIT inspection has been done previously, and found NAI or VAI, or after another Level 1 inspection which was found NAI or VAI
*** All OAI inspections should be followed by Level 3 QSIT inspections. Fatal flaw can not be used when previous inspection was OAI.

Fatal Flaw statement: WHEN THE INSPECTION IDENTIFIES SYSTEM-WIDE DEFICIENCIES THAT, IN TOTAL, MEET THE CRITERIA FOR SITUATION I IN PART V.A.1. OF THIS PROGRAM, THE INVESTIGATOR SHOULD DOCUMENT THE CONDITIONS THAT CONTRIBUTED TO THE PROBLEM(S), AND CLOSEOUT THE INSPECTION.

c. Required Statement. For all Quality System inspections the Form FDA-483 should contain the following statement:

<u>THE OBSERVATIONS NOTED IN THIS FORM FDA-483 ARE NOT AN EXHAUSTIVE LISTING OF OBJECTIONABLE CONDITIONS. UNDER THE LAW, YOUR FIRM IS RESPONSIBLE FOR CONDUCTING INTERNAL SELF-AUDITS TO IDENTIFY AND CORRECT ANY AND ALL VIOLATIONS OF THE QUALITY SYSTEM REQUIREMENTS</u>.

2. <u>Inspectional Instructions</u>

a. Quality System/GMP inspections should be conducted using the Quality System Inspection Technique (QSIT). Guidance for "how to" perform the inspections is provided in the Guide to Inspections of Quality Systems, also called the QSIT Guide. Some programs are considered satellites to the major quality subsystem areas:

Major Quality Subsystems/GMP areas
Management Controls
Design Controls
CAPA Controls
Production & Process Controls

CAPA Satellites
MDR
Corrections & Removals

Tracking

Production & Process Control Satellite
Sterilization

Refer to the QSIT Guide for details on how to inspect for those areas mentioned above. **Refer to Parts V of this Compliance Program for guidance on Regulatory and Administrative follow-up to those programs.**

b. When to inspect for the programs.

Use the following guidance for determining when to cover the various programs which are mentioned in section "a" above. **Use the QSIT Guide for "how" to inspect those areas.**

Quality Systems/GMP. Coverage is determined by the "level" of inspection. See Part III, section A.1 for guidance on which level to use, and thus which subsystems to inspect.

MDR. An MDR inspection should be conducted each time a Level 2 Quality System/GMP inspection is done. A MDR inspection should also be initiated when complaints involving a death(s) or serious injury (s) are reported, or when a Level 1 inspection finds CAPA violations.

Corrections & Removals. A Corrections & Removals inspection should be conducted each time a Level 2 Quality System/GMP inspection is done. A Corrections & Removals inspection should also be initiated when a manufacturer is reporting corrections & removals of their devices on their MDR or Part 806 reports. You should make this determination each inspection. Attachment G provides further information on this program.

Tracking. A Tracking inspection should be conducted each time a Level 2 Quality System/GMP inspection is done.

Sterilization. A Sterilization inspection should be conducted when you are inspecting a contract sterilizer, or when you choose sterilization as the "process" for review under the production & process controls section of QSIT. Sterilization does not need to be covered during each quality system inspection.

3. Registration and Listing

For specific guidance concerning device registration and listing requirements see IOM Subchapter 770 – Regulatory Submissions, section 772.1 Device Registration and Listing.

4. Sample Collection

For QS/GMP, MDR, Tracking and Correction and Removals violations, documentary samples are not necessary for Level 2 inspections and for warning letters. However, these samples may be needed for Level 3 inspections as per instructions from the case officer.

Physical samples are generally not required to support QS/GMP violations, and should not be routinely collected for QS/GMP cases. If the district should reference violative documentary or physical samples as evidence to support QS/GMP deviations, the condition of the sample should be tied to the QS/GMP deviation to show a cause/effect relationship.

Normally, the collection of samples for sterility issues is not to be performed during Level 1 (Abbreviated) inspections of device manufacturers or contract sterilizers. The following items provide guidance on sampling decisions. Should you have questions regarding the need to collect samples related to the sterilization process, you should contact Sarah Mowitt at (301) 594-4595.

- Finished device samples are not to be collected and tested for sterility to prove quality system deficiencies in sterilization validation or process control. Under certain circumstances, the Center may request that samples be collected for sterility testing. In such cases, collect 132 devices from a lot unless the lot size is small or the cost is prohibitive. If 132 devices are unavailable because of lot size or cost, contact the analyzing lab to determine the minimum number of devices that should be collected.

- Packaging samples are to be collected for laboratory confirmation of defective packaging found during a visual field examination of packaging if regulatory action is contemplated for packaging deficiencies. The sample is to consist of 20 sterilized packaged devices.

- Bioburden samples are to be collected only 1)when your review of the results of bioburden testing performed by the manufacturer finds unrealistically low results, and 2) the sterilization process is a bioburden based cycle with no safety overkill element. The sample is to consist of 20 unsterilized devices.

- Biological indicators are not to be collected routinely. Collect fifty biological indicators only if you have reason to question the effectiveness of the indicators or under direction by the Center.

- Endotoxin samples are to be collected only when endotoxin control is necessary for the device and when your review of the manufacturer's test methodology leads you to believe that the manufacturer's test results may be unrealistically low. Collect 10 sterilized devices.

- Field examination of packaging used for sterile devices may be indicated when your assessment of packaging operations demonstrates a lack of control such that inadequate packaging is likely to occur. Examine the packages for integrity of the sterility barrier, paying close attention to seals. Use the sampling tables in the QSIT Guide to determine sample size.

If the investigator is uncertain as to whether a sample should be collected, the district should consult with the CDRH Headquarters Laboratory Liaison or the Division of Field Science in ORA on the laboratory capability to conduct the analysis. (See Part VI, C. for program contacts).

5. Follow-up Inspections

See Part V, Section A. 5. b. for guidance.

6. Foreign Inspections

All foreign inspections should be conducted using the QSIT Guide and at the appropriate Inspection Level as defined by the inspection assignment.

NOTE: For all foreign inspections, use the same PACs as those used for domestic inspections, i.e., 82845A, B, C, or G, etc., as appropriate.

Special Note: **PAC 82R806 is now obsolete.**

B. SPECIAL SITUATIONS

1. For Cause Inspections

For Cause inspections can still be conducted as the need arises. These inspections are generally more in-depth than the QSIT inspections. These inspections should be directed towards finding the quality problems, tracing the root causes and assuring the appropriate corrective and preventative actions are initiated. For Cause inspections are usually initiated as a result of CDRH, ORA headquarters, Regional or District directives. These inspections are but not limited to: follow-up to recalls, consumer complaints, defective products, etc. Immediate investigations/inspections are needed in these cases. These inspections can be conducted using the QSIT Guide, however, often more in-depth investigations are needed in the CAPA area.

"For cause" inspections may also be initiated at a contract sterilizer when an inspection of a device manufacturer raises questions about the adequacy of processing or quality assurance by the contract sterilizer. Likewise, an inspection of a contract sterilizer may lead to a "for cause" inspection of device manufacturers if significant deficiencies observed at the contract sterilizer might be an indication that the device manufacturer has not assumed appropriate responsibility for the sterilization validation and processing of its own devices. The district that has identified the need for the additional coverage is to notify the home district of the establishment that needs a "for cause" inspection.

2. Special Instructions Concerning Design Controls

The inspectional authority for review of design control records is derived from Section 704(e) of the Act. Such authority applies only after the establishment has manufactured the device for which the design has been under development or taken an action that precludes the argument that the product under development is not a device. Such action includes: (1) submitting to an IRB plans for clinical investigation of the device, (2) submitting to FDA a Product Development Protocol (PDP), (3) submitting to FDA an IDE, 510(k), or PMA, (4) change to an already marketed device, or (5) refer to Attachment D for decision charts outlining when FDA has inspectional authority to review design control records.

THE ABOVE LIMITATION DOES NOT APPLY TO INSPECTIONAL AUTHORITY TO REVIEW ALL GENERIC DESIGN CONTROL PROCEDURES

AT ANY POINT IN TIME.

Review of design controls should cover any design processes after June 1, 1997. The establishment is not required to retrospectively apply design controls to any stages in the design process that it had completed prior to June 1, 1997.

If an establishment normally designs its own devices, but has not initiated any design changes to current devices or does not have a design project underway that is reviewable by FDA given the limitation discussed above, investigators should limit their coverage to a review of the design control procedures that the establishment must have defined and documented.

There are a number of multi-establishment firms that conduct all design activities at a single facility (sometimes referred to as a research and development (R&D) center or corporate design facility). If the establishment scheduled for inspection is serviced by an R&D center or corporate facility, review the establishment jacket, consult the agency's on line OEI databases and/or direct calls to the district involved. Determine if the home district of the R&D center or corporate design facility has conducted a design control inspection of that facility within the previous two years. If such an inspection was conducted, it will not be necessary to conduct a design control assessment at the establishment scheduled for inspection. If an inspection was not conducted within the previous two years, issue an assignment to the home district of the R&D center or corporate design facility requesting a design control inspection.

Some establishments have their devices designed under contract. The establishment must comply with the requirements for using consultants under 21 CFR 820.50 as well as ensure compliance with 21 CFR 820.30. It must maintain copies of a Design History File for any device that is in production.

The observations that are placed on the FDA-483 should be limited to the adequacy of the procedures and/or controls established by the firm. Do not place observations on the FDA-483 that concern the adequacy, safety, or efficacy of a particular design. Any such concerns should be noted in the EIR and the EIR flagged for review by the Office of Device Evaluation.

3. Special Instructions for Sterilization Processes

NOTE: Sterilization inspectional guidance is found in the QSIT Guide.

Effective upon issuance of this compliance program, sterilization processes will no longer be inspected under separate compliance program circulars. (Sterilization checklists are now obsolete) The previous compliance program circulars 7382.830A (Sterilization of Medical Devices) and 7382.830B (Contract Sterilizers) are replaced by instructions in this compliance program and in the Sterilization Process Controls section found in the QSIT Guide. This coverage is a sub-part of the Production and Process Controls subsystem. The instructions for inspecting sterilization processes are applicable in the following types of facilities:

- device manufacturers that sterilize their own product;
- device manufacturers that use contract sterilizers; and,
- contract sterilizers.

NOTE: The portion of the inspection spent covering sterilization processes should be reported under PAC 82845S.

Refer to Part III, A. 4, for guidance on collection of samples relating to sterilization issues.

4. Inspection of Radiation Emitting Devices

When conducting QS/GMP inspections of radiation emitting devices, investigators should also inspect for compliance with any applicable standard promulgated under Chapter V, Subchapter C - Electronic Product Radiation Control of the FD&C Act.

Device manufacturers subject to existing FDA performance standards (21 CFR Parts 1010 – 1050) should include in their device master and history records those procedures and records demonstrating compliance with the applicable standard.

5. Implantable and Life Sustaining Devices (Formerly Critical Devices)

Under 21 CFR 820.65, the requirements for devices and component traceability applies to implantable devices and life sustaining devices. See Attachment B for a list of such devices. (Note: this list may not be comprehensive. The definition specified in 21 CFR 820.65 should be used when determining if these requirements must be met.)

6. Comparison of Requirements Between the 1978 GMP Regulation and the 1996 Quality System Regulation

While the QS/GMP requirements that apply to manufacturing are similar in both regulations, some of the requirements were reworded or otherwise modified to better harmonize with ISO 9001. See the The FDA and Worldwide Quality System Requirements Guidebook for Medical Devices, page 5 for a chart comparing the requirements in the old and new regulations.

7. FDA Compliance Status Information Systems (COMSTAT)

a. When selecting specific manufacturing processes to represent profile classes, investigators should give preference to processes that are used in the manufacture of higher risk devices; that have had problems as indicated by evaluation of the Corrective and Preventive Action Subsystem (CAPA); that present a higher risk of causing device failure; that are used in manufacturing multiple devices; with which the firm is unfamiliar or lacks experience; or that cover a variety of process technologies and profile classes. A list of the device related profile classes appears in the current FDA COMSTAT Manual. NOTE: If all profile classes are not directly covered during an inspection, but are covered indirectly under CAPA, then all profile classes the firm is involved with can be listed on the Profile Data Sheet.

b. Inspections conducted under a COMSTAT assignment should include:

(1) coverage of the device(s) specified in the assignment, or devices and related manufacturing processes representing all the same profile classes as the assigned device; and

(2) other devices as required to provide coverage of any remaining profile classes, except QS/GMP exempt Class I devices.

c. Since the QSIT approach covers "systems" in at least three of the four subsystems (production & process controls are the exception) you can apply the finding from the inspection to all profile classes at this firm.

Note: One exception exists to the above rule - If the **only** violations found were in the area of production and process controls, you should profile the inspection according to the profile class covered in that production and process. Most inspections, however, will include coverage of other profile classes due to your coverage of other subsystems.

8. Imports

No import wharf examinations or sample collections are scheduled under this program.

9. Exports

The FDA Export Reform and Enhancement Act of 1996 amended Section 802 of the FD&C Act to allow an establishment to export an unapproved device to any country that authorizes importation of the device without first obtaining FDA authorization, provided that the device has received marketing authorization from one of the countries referred to in Section 802(b)(1). Section 802 also requires that any such device must be manufactured in "substantial" conformance with the QS/GMP requirements.

Firms must notify FDA when they make the first shipment of an unapproved device. CDRH has sent copies of the notification letters to the districts for inclusion in the firm's file jacket. During the inspection, the district should confirm that the establishment has subjected the device(s) to substantially the same quality system used for devices sold domestically. In the event that Situation I conditions are identified, investigators should contact HFZ-305, Attn: Wes Morgenstern.

Otherwise, Class I & II devices that are manufactured in the U.S., but not marketed in the U.S., are not subject to the QS/GMP requirements, provided that the manufacturer has documented proof that its devices are offered for sale only in foreign countries.

C. REMARKETED DEVICES

1. Remanufacturers of Used Devices

Remanufacturers are persons who process, condition, renovate, repackage, restore or do any other act to a finished device that significantly changes the finished device's performance or safety specifications or intended use [21 CFR 820.3(w)]. Remanufacturers are considered to be manufacturers, and are subject to all applicable requirements of the Quality System regulation, MDR requirements, Device Tracking requirements,

registration and listing, and premarket clearance. If an establishment disputes its regulatory status, the district should refer the EIR to the appropriate Division of Enforcement within OC for assistance in interpreting the definition of a remanufacturer.

NOTE: For a discussion of the above issues see Federal Register Notice: December 23, 1997 (Volume 62, Number 246), pages 67011 – 67013.

2. Third Party Refurbishers/Reconditioners/Servicers of Used Devices

Third party refurbishers, reconditioners, servicers and "as is" resellers of used devices are currently not subject to the requirements of the Quality System regulation. In 1997, FDA published an Advanced Notice of Proposed Rulemaking (ANPR) requesting public comments/proposals on regulation of third party refurbishers, reconditioners, servicers and "as is" remarketers of used devices. If the district receives an assignment to inspect such an establishment, the district should contact Wes Morgenstern (HFZ-305) at 301-594-4699 to determine the current regulatory status of such establishments.

3. Reprocessors of Single Use Devices

Third party reprocessors of single use devices are considered to be manufacturers and are subject to those requirements of the Quality System regulation that apply to the operations they perform. Because contractual arrangements with hospitals and questions of ownership may sometimes make the responsibilities of the third party unclear, the district should contact Larry Spears (HFZ-340) at 301-594-4646 for guidance before conducting an inspection of an establishment believed to be a third party reprocessor of single use devices. Hospitals that reprocess/reuse single use devices for their own use are not subject to registration and listing requirements or Abbreviated inspections.

D. REPORTING

1. General Reporting requirements are listed on the cover page. As a general rule, the time used for preparing for the inspection and writing the EIR should not exceed one half (1/2) the time spent conducting the inspection.

2. Quality System/GMP Observations--If you observe any violations of the QS/GMP requirements, you should place them on the Form FDA-483. The QSIT Guide provides guidance concerning major QS requirements and the identification of major deviations. The most serious system deficiencies should be noted on the Form FDA-483 first. Special Note: Refer to IOM, Section 512.1, 8 for information concerning annotation of the Form FDA-483.

3. 510(k) Observations--If the establishment does not have a substantially equivalent 510(k) for a device, or has made significant changes that require a new 510(k), investigators should not place the observations on the Form FDA-483 unless you obtain concurrence from CDRH/OC. Refer to existing policy in the IOM, Section 512.1, 15.

4. Registration and Listing Observations—If a firm has failed to list device(s) or update listing every six months as required by 21 CFR Part 807, you should place the

observations on the Form FDA-483. NOTE: Do not cite an establishment for failure to reregister unless it has not done so for two or more years.

PART IV

ANALYTICAL

A. ANALYZING LABORATORIES

The district will make all the necessary arrangements for proper handling of samples with the following designated testing facilities:

TYPES OF DEVICES	ANALYZING LABORATORIES
All General Medical Devices	Winchester Engineering and Analytical Center (WEAC) 109 Holton Street Winchester, Massachusetts 01890-1197
Radioimmunoassay	W E A C
All Other In Vitro Diagnostic Devices	Micro—WEAC Chem—WEAC
Testing for sterility of finished devices, package integrity, bioburden, and endotoxins:	WEAC
Testing of biological indicators:	Central Laboratory for Microbiological Investigations (CLMI) 240 Hennepin Avenue Minneapolis, Minnesota 55401-1912

See PART VI regarding those persons designated as contacts for designated laboratories and specific products.

B. ANALYSES TO BE CONDUCTED

Sample collection and analysis will be determined on a case-by-case basis through consideration of inspectional findings, compliance and scientific capabilities and expertise. Full collaboration between investigations and analytical personnel is essential at this phase. See Part III, A, 4 for additional information.

C. METHODOLOGY

1. Testing Finished Device Samples for Sterility

a. Visually examine each unit to ascertain that its packaging is intact. Report all defects observed by describing the size, type and location of the defects. Units with defective packaging need not be examined for sterility.

b. Finished device samples are to be tested in accordance with the requirements of USP 23 methodology for Sterility Tests. **Reference the FDA Sterility Analytical Manual for guidance on applying the USP methods.**

c. Device samples are to consist of 132 units, as follows:

30 units tested in Soybean-Casein Digest Broth
30 units tested in Fluid Thioglycollate Broth
60 units for re-test, if required under USP methodology
10 units for bacteriostasis/fungistasis testing
2 units for system control

When 132 units are not available because of lot size or cost, follow the USP 23 recommendations for the minimum number of articles to be tested in each media, as follows:

Number of Articles in the Batch	Number of Articles to be tested
Not more than 100 articles	10% or 4 articles, whichever is greater
More than 100, but not more 500 articles	10 articles
More than 500 articles	2% or 20 articles

Note that the USP permits the division of articles into equal portions for addition to each of the specified media when the contents of the article are of sufficient quantity (see USP 23 to determine what is a sufficient quantity).

NOTE: For the purposes of this compliance program, the "articles" referred to in the USP may be interpreted as devices.

d. Positive subsamples

Check cultures for growth daily and begin qualitative analysis of growth immediately upon detection of growth. Follow subculturing procedures in the Sterility Analytical Manual. Continue to incubate growth vessels after subculture for full term analysis to detect slow growing bacteria and molds. For each subsample found to be non-sterile, prepare a pure culture of each contaminant.

All isolates from sterility tests must be maintained until otherwise notified by CDRH or for one year.

2. Presterilization Microbial Contamination (Bioburden)

Bioburden testing is to be performed in accordance with the guidance provided in ISO 11737-1, Sterilization of medical devices - Microbiological methods - Part I: Estimation of population of microorganisms on products. The methodology used for estimating the bioburden is to be validated. Twenty units are to be tested.

3. Analysis of Biological Indicators

Test 50 biological indicators according to USP 23 using sterilization conditions specified on the indicator label. Normally, survival-kill methodology is to be used. Under some conditions, the D-value may also be determined. In these cases, the determination will be performed according to the claims of the manufacturer of the indicator or inoculated product.

4. Analysis of Packaging Defects

Perform a visual, non-destructive, inspection of the package noting the existence and location of seal or material defects. Normally 20 packaged devices will be collected for analysis. Further testing is to be performed using consensus standards such as those identified in the Part VI.A.1 references for the American Society for Testing and Materials (ASTM). Selection of the test will depend on the materials and construction of the package, and on the nature of the noted or suspected problem.

5. Analysis of Endotoxins

Samples will be analyzed using the Bacterial Endotoxins Test found in USP 23 and the Sterility Analytical Manual. Ten units are required for endotoxin testing.

PART V

REGULATORY/ADMINISTRATIVE FOLLOW-UP

FDA staff should not deviate from the guidance in this Part without appropriate justification and supervisory concurrence.

A. QUALITY SYSTEM/GMP REGULATORY/ADMINISTRATIVE FOLLOW-UP

1. Compliance Decision

a. Situation I

The district has evidence indicating that one or more **major nonconformities** with the Quality System regulation has resulted in the inspection being classified as OAI. Examples of deviations that may be considered **major nonconformities** include:

- Total failure to define, document, or implement a quality system or one of the seven subsystems, for example, absence of Management Controls Subsystem.
- A **major deficiency** in one or more element(s) of the subsystems. The QSIT Guide provides guidance addressing what are major Quality System requirements. See Chart A for seven specific examples, one from each subsystem. Please note there are other possible deficiencies that would support an OAI determination. Examples are provided for illustrative purposes only.
- The existence of products which clearly do not comply with the manufacturer's specifications and/or the Quality System regulation and which were not adequately addressed by the Corrective and Preventive Actions Subsystem (CAPA) program.
- Noncorrection of **major deficiencies** from previous inspection(s).
- An excessive number of minor nonconformities against the Quality System requirements, either found in more than one subsystem or that are repeat deficiencies that may be indicating a trend, and uncorrected could become a **major nonconformity**, or could be related to potential product failures.

OAI: The determination of OAI should be based on evidence of Quality System, or subsystem(s) deviations, which constitute one or more **major nonconformities**.

CHART A

The examples of Situation 1 violations below are for illustrative purposes only. There are many other possible examples.

Management Controls Subsystem

- 820.20(c)
  Management with executive responsibility did not conduct management reviews at defined intervals and with sufficient frequency to evaluate the suitability and effectiveness of the quality system.

Design Controls Subsystem

- 820.30(g)
  Design validation did not ensure that devices conform to defined user/patient needs and intended uses.

Production and Process Controls Subsystem

- 820.70(a)(2)
  Process parameters and component and device characteristics are not monitored and controlled during production.

Corrective and Preventive Actions Subsystem

- 820.100(a)(1)
  Not all sources of quality data are analyzed to identify existing and potential causes of nonconforming product and other quality problems.

Facilities and Equipment Controls Subsystem

- 820.70(g)
  Equipment used in the manufacturing process does not meet specified requirements.

Document, Records, and Change Controls Subsystem

- 820.40(a)
  Documents that were not approved were observed at a location where they were being used.

Material Controls Subsystem

- 820.160(a)
  Procedures for the control and distribution of finished devices were not defined, documented, implemented, and followed to ensure that only devices approved for release are distributed.

If any of these major nonconformities exist, the district is expected to classify the EIR as OAI, and based on the significance (risk) of the device, and the findings, the district should consider administrative and/or judicial action. Such actions include, but are not limited to, a warning letter[1], injunction, detention, seizure, civil penalty and/or prosecution. See Regulatory Procedures Manual for further guidance.

If any of these deviations exist for foreign manufacturers, based on the significance (risk) of the device, and the findings, a Warning Letter and/or Warning Letter with Automatic Detention will be considered by CDRH/OC.

IMPORTANT NOTE: If a serious health hazard is identified, and the firm is not cooperative in conducting a voluntary recall, an FDA mandated recall (Section 518 of the FD&C Act), administrative detention/seizure or injunction should be considered as the initial action to bring the situation under prompt control.

b. Situation II

The inspection documents QS/GMP deviations of a quantity and/or type to conclude that there is minimal probability -- in light of the relationship between quality system deviations observed and the particular product and manufacturing processes involved -- that the establishment will produce nonconforming and/or defective finished devices. The Form FDA-483, Inspectional Observations, will serve to inform the establishment of any objectionable findings.

The presence of quality systems deviations which have a low probability of leading to an unsafe or ineffective device will not warrant recommendation of an administrative and/or regulatory action.

2. Sampling Records

The Guide to Inspections of Quality Systems, also called the QSIT Guide includes instructions for sampling records for review. Sampling is an important tool for reducing the time spent reviewing records while being able to make statistically based inferences about what the findings mean.

During Level 1 and 2 inspections an investigator can terminate review of the sample if objectionable conditions are observed before the entire sample is reviewed. The investigator can make the FDA-483 observation that the objectionable condition was found and move on to the next part of the inspection. However, QSIT Guide instructions caution that not reviewing the entire sample may result in the loss of additional information useful in understanding the potential prevalence of the objectionable condition or the failure to find other objectionable conditions.

During Level 3 inspections, however, the investigator and the compliance officer should work together closely to plan how sampling will be conducted. It is important for the

[1] Before issuance of Warning Letters, consult the Medical Device Warning Letter Pilot. [Federal Register Notice: March 8, 1999 (Volume 64, Number 44)] The Warning Letter Pilot can also be found on the ORA web site at http://www.**fda**.gov/ora

compliance officer to be confident that the level of sampling will be sufficient to support a legal action. During Level 3 OAI follow-up inspections, it is recommended that the investigator review the entire sample of records to provide a complete picture of any deficiencies identified during sampling. The EIR should reflect the following information:

- The type of records reviewed;
- The sampling table used, Table 1 or 2;
- The row used, row A, B, C, D, E or F;
- The size of the sample;
- The number of records actually reviewed (may be the same as or different from the size of the sample); and
- The results of sample review.

Statistical support is available from CDRH, Office of Surveillance and Biometrics.

3. Contract Sterilizers and Device Manufacturers – Deciding Responsibility When Taking Regulatory Action

a. The following is provided as guidance for deciding which party is to be held responsible when a device manufacturer uses a contract sterilizer to perform terminal sterilization on its devices:

- o Contract sterilization is considered an extension of the finished device manufacturer's process. The manufacturer is ultimately responsible for assurance that validation, sterilization operations, and quality assurance checks used for its products are appropriate, adequate and correctly performed.

- o Contract sterilizers are considered manufacturers for the purpose of applying the Quality System Regulation in that they meet the definition in Section 820.3(o). Contract sterilizers are subject to those parts of the Quality System Regulation that apply to the manufacturing operations they perform for finished device manufacturers.

- o While the finished device manufacturer bears overall responsibility for the safety and effectiveness of the device, both the contract sterilizer and the finished device manufacturer are legally responsible for an effective sterilization process. The written agreement required by 21 CFR 801.150(e) may be referenced to determine how the two parties have defined their respective responsibilities.

b. When there are violations, regulatory actions should reflect the shared responsibility between the contract sterilizer and finished device manufacturer. In some situations, it may be appropriate to initiate regulatory action against both the contract sterilizer and the device manufacturers (customers):

- o Action should be considered against the contract sterilizer in areas for which it has the prime responsibility under the written agreement. It may be necessary to inspect one or more customers to develop supporting

documentation when the particular sterilization firm appears not to have adequate overall process controls.

- When an inspection of a contract sterilizer finds violations in areas that are the responsibility of the finished device manufacturer (such as validation, biological indicators, package seal testing, etc.), these violations are to be reported to the home district of the manufacturer. Regulatory action consistent with the action of choice for the contract sterilizer should be considered for the finished device manufacturer.

- Because the finished device manufacturer is ultimately responsible for the contractor's activities, serious deficiencies in the contract sterilization operations will probably indicate consideration of regulatory action against the device manufacturer also. Copies of Warning Letters issued to the contract sterilizer should be sent to the home districts of the finished device manufacturers for placement in the firm's jacket. These documents should be used as a basis for the next scheduled inspection of the device manufacturer. However, when a possible health hazard exists due to the contract sterilizer's operation; or, an administrative or legal action is contemplated against a device processed by the contract sterilizer, the home district of the finished device manufacturers should schedule an immediate follow-up inspection of all affected device manufacturers.

4. Violative Devices Sold to Government Agencies

Agency policy requires that products sold to the federal government shall be treated in the same manner as products sold to commercial accounts. Consequently, when FDA recommends against acceptance of a device by a government agency because that device, or its manufacturer, is in violation of the FD&C Act, FDA shall also include appropriate regulatory/administrative action against the same or similar device sold to commercial accounts.

If an establishment has shipped a violative product to a Government agency, regulatory action consistent with the nature of the violation(s) may be taken even though there have been no shipments to commercial customers. Formal regulatory action in connection with a violative shipment may not be necessary in some cases. For example, the establishment promptly corrects the violative condition, and existing Agency policy would not require further action if the matter involved a product shipped to a non-government customer. However, where corrections are not or cannot be made promptly, the main concern is preventing the subsequent shipment of the product to another customer. When the product has been shipped solely to a Government agency and is under control of that agency and there is no threat to the public, the ORA/Medical Products Quality Assurance (MPQA) staff shall ascertain the intention of the agency holding the goods (e.g., will they return or destroy the goods; will they request FDA to initiate seizure, etc.). If the procuring agency requests FDA action, the ORA/MPQA staff will refer the matter to the home district for their consideration of an appropriate recommendation.

5. Administrative and Judicial Actions

Actions which may be considered include FDA requested recall, FDA mandated recall, Warning Letter, seizure, injunction, prosecution, civil penalties and detention.

Corrective action proposals should be submitted by a responsible official of the establishment in writing, detailing the action(s) to be taken to bring the violative process or product into compliance within a specified time frame. Voluntary correction does not preclude the initiation of administrative and/or judicial action.

Special Note: Please review Warning Letter Pilot when reviewing corrective actions.

In determining whether quality systems deviations are sufficient to support legal action, consideration should be given to the significance of the device, the establishment's quality history, and whether the problem is widespread or continuing.

When CDRH does not agree with a district's recommendation for a regulatory action, the district will be notified of the reasons for disapproval in writing.

a. Warning Letters

Issuance of all Warning Letters should follow Chapter 4 of the Regulatory Procedures Manual (RPM) (see Attachment C for Model Warning Letters). Districts have DIRECT REFERENCE AUTHORITY for Warning Letters for quality system violations, with the exception of design control violations under 820.30.

Districts should obtain CDRH concurrence before issuing Warning Letters related to refurbishing/reconditioning of used devices, or reprocessing of single use devices .

If the district determines that issuance of the Warning Letter has resulted in corrective action by the establishment, the district should, within five (5) working days after confirmation, update the establishment's Profile Data Sheet.

b. Violative Follow-Up Inspections

As stated in Part III of this Compliance Program, the post-inspection activities serve to advise manufacturers that the conditions identified by the investigator may be symptomatic of system problems, and that the manufacturer is responsible for investigating, identifying, and correcting system problems. The model Warning Letters further direct the establishment to discuss in its response how it will address the system problems related to the conditions identified by the investigator.

After issuance of a Warning Letter for Quality System violations the next inspection should be a Level 3 inspection, as explained in Part III. When investigators identify the same or additional conditions that meet the criteria for Situation I (note: deficiencies in the performance of self-auditing are considered a criteria for Situation I at the follow-up inspection stage), the district should consider higher level enforcement actions, such as seizure, injunction, or civil

penalties. During Level 3 QSIT inspections, the investigator should work closely with the compliance officer to assure the appropriate coverage is provided.

c. The Recidivist Policy -- Enforcement Strategy For Establishments With Repeated Violative Inspections

(1) Some establishments have a high rate of recidivism. They have developed a pattern of correcting violative conditions in response to Warning Letters or other administrative/regulatory actions, and usually maintain those corrections long enough to pass the follow-up inspection. When FDA next inspects the establishment (sometimes, as a follow-up to a recall), the investigator identifies similar conditions that again meet the criteria for Situation I. This tendency toward recidivism is often due to the failure of the establishment to have a strong quality policy and basic manufacturing and quality assurance systems which meet the requirements of the Quality System regulation.

(2) When dealing with another violative inspection for such an establishment, the district should consider using the following strategy:

(a) Issue a Warning Letter that follows the model Warning Letter in Attachment C. This Warning Letter requests the manufacturer to submit to the district (for up to 2 years if the district believes that it is necessary) an annual certification by an outside expert consultant stating that it has conducted a complete audit of the establishment's manufacturing, quality assurance (and if applicable, design control) systems relative to the requirements of the Quality System regulation. The establishment should submit a copy of the consultant's report[2], and certification by the establishment's CEO that he or she personally has received and reviewed the consultant's report and that the establishment has made all corrections called for in the report. To keep the process on track, schedules, milestones, update reports and other similar activities should be established after issuance of the Recidivist Warning Letter.

(b) Compliance Officers have the option of limiting the review of the certification only to the extent necessary to confirm that the consultant and the establishment have met the requirements set forth in the Warning Letter. Compliance Officers may also request a technical evaluation of the consultant's report by the appropriate branch within the Office of Compliance (OC). Compliance Officers have no obligations, however, to send to the establishment comments regarding the adequacy of the consultant's report or the establishment's corrections.

[2] Establishments may be asked to release consultant's reports as part of their voluntary agreement with FDA. Because of its voluntary nature, the request is not in conflict with 21 CFR 820.180(c).

(c) Follow-up inspections will normally be conducted 3 – 6 months after the establishment certifies that it has completed all corrections.

The district may update the profile data sheet as soon as the establishment has certified that it has completed all corrections recommended by the consultant.

(d) If the follow-up inspection indicates that the corrections are satisfactory, the district should notify the establishment that it has no objections to the corrections, and remind the establishment that it should continue to submit to the district, on the schedule specified in the Warning Letter, certification by an outside expert consultant that it has conducted an updated audit, certification by the establishment's CEO that any corrections noted to be necessary by the consultant have been made, and that it remains in compliance with the requirements of the Quality System regulation. The establishment should continue to submit copies of the audit results.

(3) If conditions identified by the follow-up inspection meet the criteria for Situation I, the district should consider action per A.1. above.

(4) If the evidence indicates that the consultant's or establishment's certifications are fraudulent, the district is encouraged to request participation by the Office of Criminal Investigations. When there is clear evidence that the establishment falsified its status report to the district, the district should initiate appropriate charges under 18 USC, 1001.

d. Recalls

If the district believes that prompt removal of a violative product from channels of commerce is necessary, it should proceed in accordance with established recall procedures in Chapter 7 of the RPM and 21 CFR, Part 7 (Enforcement Policy), Subpart C (Recalls). In the event there exist serious adverse health consequences or a death, CDRH may order discontinuation of distribution and recall of a device to the user level in accordance with Section 518(e) of the Act.

e. Administrative Detention/Seizure

Prior to approving an administrative detention, the district director should have reason to believe the device is misbranded or adulterated and the establishment holding the device is likely to quickly distribute or otherwise dispose of the device, or detention is necessary to prevent use of the device by the public until appropriate regulatory action may be taken by the Agency. District directors should consult with CDRH by telephone, contacting the appropriate Case Expert/Division Director in OC for the subject device by consulting the list of Case Experts and/or the CDRH/OC organization chart, both of which can be found in Part VI, C. Program Contacts. Concurrence should be given by the Director, OC, CDRH, based on a recommendation by the OC staff.

The district should immediately recommend a seizure.

A seizure action can be recommended without administrative detention to remove violative devices from commercial distribution, either at the manufacturer, distributor, repacker or a device user location.

f. Injunction

If an establishment has a continuing pattern of significant deviations in spite of past warnings, injunction will usually be the recommended action of choice. If a serious health hazard exists, the recommendation should include a request for a temporary restraining order (TRO) to prevent the distribution of devices that have been manufactured under the violative conditions documented by the inspection report (see RPM Chapter 6). The recommendation should be accompanied by copies of all necessary documents, e.g., complete inspection reports, Warning Letters issued, sample analyses reports, establishment's response(s) to Warning Letters and/or Form FDA-483. In the absence of samples, the inspectional evidence should clearly show that the establishment has substantially deviated from the requirements of the Quality System regulation. These deviations should be well documented and should show system deficiencies, not just an isolated event.

g. Citation

A citation should be recommended if appropriate as stated in Chapter 5 of the RPM.

h. Prosecution

The criteria stated in Chapter 6 of the RPM are the criteria for consideration of prosecution of individuals in violation of the requirements of the Quality System regulation.

i. PMA Disapproval/Withdrawal

Refer to Compliance Program 7383.001, Part V.

j. Automatic Detention

In general, detention should be recommended by the Office of Compliance whenever there is clear documented evidence to suggest that the foreign manufacturer is producing or is likely to produce nonconforming and/or defective devices or the device presents a hazard to health.

k. Civil Money Penalties

Section 303(f)(1)(B)(i) of the Act states that civil money penalties shall not apply to QS/GMP violations “unless such violation constitutes (I) a significant or knowing departure from such requirements, or (II) a risk to public health.” Section 303(f)(1)(B)(iii) further stipulates that civil penalties shall not apply to

"section 501(a)(2)(A) which involve one or more devices which are not defective." Policy is still being developed for use of civil penalties in violative QS/GMP situations. It is, therefore, important for districts to consult with CDRH/OC before committing resources to developing such recommendations.

6. Facilitating Review of Regulatory Recommendations

a. The district should contact the appropriate CDRH/OC Case Expert/Division Director by phone when the district believes they have an OAI situation for which a recommendation for seizure, injunction, civil penalties, or prosecution may be appropriate. At the discretion of the district, notification to CDRH may occur prior to an inspection, while the inspection is ongoing, or after issuance of the FDA-483. Notification would typically be made by a compliance officer, but could be made by the investigator and/or district management. A list of the Case Experts, their phone numbers, and respective Device Panel responsibilities, are shown in PART VI, C. Program Contacts. The CDRH/OC organization chart also shown in PART VI, C. Program Contacts should be consulted for Division Director identification.

b. When the district knows a regulatory action will be forthcoming as a result of the inspection, it should FAX a copy of the issued Form FDA-483 to the appropriate division in OC. The review process can begin within CDRH while the EIR and recommendation are being written by the district. A copy of the Form FDA-483 annotated with exhibit numbers, and EIR page numbers, helps the reviewers.

c. It is the responsibility of district management to ensure that the documentation and evidence presented with each legal action recommendation is sufficient to justify each charge. The volume of material submitted should include only the basic documentation needed to support each QS/GMP charge/example.

d. It is essential that all necessary samples and other supporting documentation be tabbed and their location cross referenced in the recommendation in order to assist in a timely review. It is highly recommended that you provide a table that cross references the violation with the Form FDA-483 item number, the inspection report page number and the exhibit number.

e. It is essential that all significant questions, problems, or other weaknesses in the evidence regarding the recommended action be stated, along with pertinent district comments. Otherwise, reviewers may miss a problem entirely until litigation is commenced.

f. The recommendation should begin with the most serious violation of the regulations with reference to the EIR pages, exhibits and sample results which document the violation. Each charge should be parenthetically referenced in the recommendation memorandum and the page location of the supporting evidence given. Violations should be listed in decreasing order of importance. Each violation should be related to its effect on device quality in light of overall controls, and should be separated according to the type of manufacturing activity.

g. Physical samples are not required to support QS/GMP violations, and should not be routinely collected for QS/GMP cases. If the district should reference violative documentary or physical samples as evidence to support QS/GMP deviations, the condition of the sample should be tied to the QS/GMP deviation to show a cause/effect relationship.

h. Evidence of previous warning and other regulatory actions should be referenced along with a description of corrective actions. If the recommendation or current EIR references a previous report, the district should either copy the cited EIR pages, or summarize the information.

i. All legal action recommendations shall be sent to CDRH/HFZ-306 for processing.

B. MDR REGULATORY/ADMINISTRATIVE FOLLOW-UP

1. General Information

MDR violations must be fully documented in any of the situations described in item "2." below. Recommendations for enforcement actions, **other than Warning Letters concerning death and serious injury**, shall be sent to HFZ-306 for review and concurrence. If other means are used to advise a firm that they are in violation of the MDR regulation, inform HFZ-306 by forwarding copies of the Form FDA-483, memorandum of meeting, or other pertinent information.

2. Situation I

NATURE OF VIOLATION	ACTION TO CONSIDER
Firm has received prior notice and still fails to comply with the MDR regulation.	Recommend Warning Letter, Seizure, Injunction and/or Civil Penalties
Firm fails to report within five workdays of becoming aware that a reportable MDR event necessitates remedial action to prevent an unreasonable risk of substantial harm to the public health.	Recommend Warning Letter
Firm fails to submit an MDR reportable death report.	Recommend Warning Letter
Firm fails to report an MDR Serious injury report	Recommend Warning Letter
Firm fails to submit an MDR malfunction report.	Cite on Form FDA-483

Firm has not established an MDR Complaint File and/or Written Procedures.	Cite on Form FDA-483
Firm fails to investigate an MDR reportable event per 803.50(2) and 820.198.	Cite on Form FDA-483
Firm fails to obtain information necessary to file a complete death, or serious injury malfunction report.	Cite on Form FDA-483
Failure to submit or provide complete Baseline Report information.	Cite on Form FDA-483
Firm fails to submit a Supplemental report within 30 days of becoming aware of the information.	Cite on Form FDA-483

All failures should be listed on the Form FDA-483. The district should follow the guidance in the Regulatory Procedures Manual (particularly where continuing violations have been documented) when determining whether to utilize additional means of notification beyond the Form FDA-483, such as issuing a Warning Letter or setting up a conference between the firm and the district.

C. TRACKING REGULATORY/ADMINISTRATIVE FOLLOW-UP

1. General Information

Tracking violations must be fully documented in any of the situations described in item "2."

Provide HFZ-306 with a copy of any communication notifying a firm that they are in violation of the Tracking regulation, e.g., Form FDA-483, memorandum of meeting, etc. In addition, all recommendations for Tracking enforcement actions shall be sent to HFZ-306 for review and concurrence.

2. SITUATION I	ACTION TO CONSIDER
Firm has received prior notice and continues to violate the Tracking regulation.	Recommend a Warning Letter, Seizure, Injunction, and/or Civil Money Penalties.
Firm does not have a tracking system.	Recommend Warning Letter.

Firm does not have written SOPs for collection, maintenance and auditing of the data for its tracked device(s).	Recommend Warning Letter.
Firm fails to audit its tracking system within the required time frame.	Cite on Form FDA-483.
Firm's tracking system is not effective in locating tracked devices during recall/notification.	Recommend Warning Letter.
Firm does not follow its written SOPs for tracking.	Cite on Form FDA-483
Firm fails to transfer tracking records when it sells its tracked device to another firm.	Cite on Form FDA-483
Firm fails to notify FDA it is no longer in business for a tracked device	Cite on Form FDA-483

D. CORRECTIONS AND REMOVALS REGULATORY/ADMINISTRATIVE FOLLOW-UP

1. General Information

Corrections and Removals (CAR) violations must be fully documented in any of the situations described below in item "2."

Provide HFZ-306 with a copy of any communication that notifies a firm it is in violation of the CAR regulation, e.g., Form FDA-483, memorandum of meeting, etc. In addition, all recommendations for CAR enforcement actions shall be sent to HFZ-306 for review and concurrence.

2. Situation I

NATURE OF VIOLATION	ACTION TO CONSIDER
Firm has received prior notice and continues to violate the CAR regulation.	Recommend Warning Letter, Seizure, Injunction, and/or Civil Money Penalties
Firm fails to submit a CAR report.	Recommend Warning Letter.
Firm fails to submit a CAR report	Cite on Form FDA-483

within 10 working day time frame.

Firm fails to establish and/or maintain a file of unreported Corrections or Removals.	Cite on Form FDA-483
Firm fails to provide all the data required in the CAR report.	Cite on Form FDA-483

E. ELECTRONIC RECORDS AND ELECTRONIC SIGNATURES REGULATORY/ADMINISTRATIVE FOLLOW-UP

General Information

Recommendations for enforcement actions, including Warning Letters, shall be sent to HFZ-306 for review and concurrence. If other means are used to advise a firm that they are in violation of part 11, the Electronic Records and Electronic Signatures regulation, inform HFZ-306 by forwarding copies of the Form FDA-483, memorandum of meeting or other pertinent information.

Part 11 goes hand in hand with predicate rule requirements to maintain records. In regard to the Electronic Records and Electronic Signatures Regulation, a predicate rule is any FDA regulation that requires subject firms to maintain records. For example, the Quality System Regulation requires that medical device manufacturers maintain records including a device master record, device history record, design history file, and quality system record.

- Records maintained by a device manufacturer are subject to part 11 if the records are required by a predicate rule and if the records are created and/or maintained in electronic form.

- Electronic signatures are subject to part 11 if the predicate rule requires signatures or if electronic signatures are not required by the predicate rule but appear in records required by the predicate rule.

- When drafting a Warning Letter or recommendation for legal action, cite both the relevant recordkeeping requirement of the predicate rule and requirement of part 11 relevant to the deficiency.

All failures should be listed on a Form FDA-483. Part 11 is an agency-wide rule. Guidance on enforcement of Part 11 is being developed on an agency-wide basis. Look for guidance in the form of Compliance Policy Guides and training in the future. The district should follow such guidance in determining whether to utilize additional means of notification beyond the Form FDA-483, such as issuing a Warning Letter, setting up a conference between the firm and the district, or taking further regulatory action. The district should also contact CDRH for additional guidance if further regulatory action is contemplated.

PART VI

REFERENCES, ATTACHMENTS AND PROGRAM CONTACTS

A. APPLICABLE REFERENCES OR AIDS

1. Guide to Inspections of Quality Systems, June 1999.

2. Code of Federal Regulations, Title 21, Part 820 Current Good Manufacturing Practice (CGMP) Final Rule; Quality System Regulation.

3. Federal Food, Drug, and Cosmetic Act, As Amended.

4. Investigations Operations Manual - Chapter 5, Subchapter 550.

5. Biotechnology Inspection Guide, Nov. 1991.

6. Medical Device Quality Systems Manual: A Small Entity Compliance Guide (HHS Pub. No. FDA 94-4179, Dec. 1996).

7. NBS special Publication 250 - May 1984 (or update) Calibration and Related Measurement Services, U.S. Dept. of Commerce NBS, Washington, D.C. 20234.

8. Guideline on General Principles of Process Validation: Notice of Availability published in the Federal Register on May 1987.

9. Intercenter Agreement Between the Center for Biologics Evaluation and Research and the Center for Devices and Radiological Health, October 31, 1991

10. Software Development Activities, July 1987.

11. Glossary of Computerized System and Software Development Terminology, August 1995.

12. Quality Control Handbook, Juran, J.M., 3rd edition, McGraw-Hill, 1974.

13. ANSI/ASQC Z1.4 (Replaces MIL-STD 105E), ANSI/ASQC Z1.9 (Replaces MIL-STD 414) Sampling Procedures and Tables for Inspection by Attribute.

14. COMSTAT Guidance- Field and Centers: September 15, 1998.

15. Classification Names for Medical Devices and In Vitro Diagnostic Products, HHS Publication No. (FDA) 91-4246, August 1995. This directory is organized by "keywords" in alphabetical order. The classification number (5 digit product code), class, and CFR regulation number is given for each entry listed.

16. Code of Federal Regulations, Title 21, Part 809.10, Labeling for In Vitro Diagnostic Products.

17. Advisory List of Critical Devices - 1988; Notice Published in the Federal Register on March 17, 1988.

18. Overview of Metallic Orthopedic Implants; Technical report, reference material and training aid for investigators prepared by the Division Emergency and Investigation Operations (HFC-132), Office of Regional Operations, Office of Regulatory Affairs, HHS, Public Health Service, FDA, June, 1988.

19. AQL Inspector's Rule and Manual. This special purpose plastic slide rule that rigidly adheres to MIL-STD-105E can be obtained from Infor. Inc., P.O. Box 606, Ayer, MA. 01432. Phone (508) 772-0713. Cost is approximately $20 each excluding shipping and packaging.

20. Medical Device Reporting for Manufacturers, March 1997.

21. Code of Federal Regulations, Title 21, Part 821, Medical Device Tracking Requirements.

22. Do It By Design: Design Control Guidance.

23. The FDA and Worldwide Quality Systems Requirements Guidebook for Medical Devices, Compiled by Kimberly Trautman, ASQC Quality Press, Milwaukee, Wisconsin.
24. Design Control Guidance for Medical Device Manufacturers, March 1996.

25. Compliance Guide for Laser Products, September 1985 (reprinted July 1989).

26. Guide to Inspections of Electromagnetic Compatibility Aspects of Medical Device Quality Systems, Dec. 1997.

27. Guidance for Medical Gloves, A Workshop Manual, Sept. 1996.

28. IOM, Chapter 10, Reference Materials.

Copies of CDRH QS/GMP publications are available from the Division of Small Manufacturers Assistance (DSMA), Telephone: 800-638-2041 or FAX 301-443-8818.

Sources to purchase these documents:

✉ **A. National Technical Information Service (NTIS)** - For information on the NTIS system please call CDRH F-O-D (see ✉ **D.** below) and request Shelf number 3799.

✉ **B. Health Care & Industry Organizations** - For a list of organizations that have agreed to

assist in the distribution of this information please call CDRH F-O-D (see ✉ **D.** below) and request Shelf number 4799.

Sources to obtain copies free of charge:

✉ **C. World Wide Web (Internet)** - FDA/CDRH maintains a World Wide Web (WWW) site for easy access to information. The home page may be accessed via FDA's home page at **http://www.fda.gov**. For additional information on the WWW site please call CDRH F-O-D (see ✉ **D.** below) and request Shelf number 1799.

✉ **D. CDRH Facts-On-Demand (F-O-D)** - This automated fax system allows anyone to obtain CDRH information, 24 hours a day, 7 days a week by calling **800-899-0381** or **301-827-0111** from a touch-tone telephone. For additional information on obtaining MDR documents from the CDRH F-O-D system please call CDRH F-O-D and request Shelf number 5799 from DSMA Facts (press 1 at first voice prompt [VP], 2 at second VP, then follow subsequent VPs).

A. 1. APPLICABLE REFERENCES OR AIDS – SPECIFIC TO STERILIZATION

The following sources may be referenced for further guidance regarding sterilization processes:

Food and Drug Administration:

Guideline on Validation of the Limulus Amebocyte Lysate Test as an End - Product Endotoxin Test for Human and Animal Parenteral Drugs, Biological Products, and Medical Devices, December 1987.

Sterile Medical Devices. A GMP Workshop Manual. fourth Edition November 1984. Prepared by Division of Small Manufacturers Assistance, Office of Training and Assistance, HHS Publication FDA 84-4174.

Sterilization: Questions and Answers, January 1985.

A list of FDA recognized standards related to sterilization of devices may be found on the internet at www.fda.gov/cdrh/modact/steril.html.

Association for the Advancement of Medical Instrumentation (AAMI)
3330 Washington Blvd.
Arlington, VA 22201
1-800-332-2264

Biological evaluation of medical devices - Part 7: Ethylene oxide sterilization residuals (ANSI/AAMI/ISO 10993-7) 1995 (AAMI TIR 19-1998 provides guidance supplementing ANSI/AAMI/ISO 10993-7.)

Contract sterilization for ethylene oxide (TIR 14) 1997

Designing, testing and labeling of reusable medical devices for reprocessing in health care facilities: A guide for manufacturers (AAMI TIR No. 12) 1995

Ethylene oxide sterilization equipment, process considerations, and pertinent calculations (TIR 15) 1998

Medical devices - Validation and routine control of ethylene oxide sterilization - Requirements (ANSI/AAMI/ISO 11135) 1994

Packaging for terminally sterilized medical devices (ISO 11607) 1997, Supplemented by AAMI TIR 22, Guidance on application of ISO 11607 (1998)

Principles of industrial moist heat sterilization (TIR 13) 1997

Radiation sterilization – material qualification (TIR 17) 1998

Sterilization of medical devices - Microbiological methods - Part 1: Estimation of bioburden on product (ANSI/AAMI/ISO 11737-1) 1995

Sterilization of medical devices - Microbiological methods - Part 2: Tests of sterility performed in the validation of a sterilization process (AAMI/ISO 11737-2) 1998

Sterilization of health care products - Requirements for validation and routine control- Industrial moist heat sterilization (ANSI/AAMI/ISO 11134) 1994

Sterilization of health care products - Requirements for validation and routine control - Radiation sterilization (ANSI/AAMI/ISO 11137) 1995

Sterilization of health care products - Substantiation of 25 kGy as a sterilization dose for small or infrequent production batches. (ISO/TR 13409) 1996

Federal Standard Airborne Particulate Cleanliness Classes in Cleanrooms and Clean Zones, 9/11/92, Fed. Std. No. 209E.

ANSI/ASQC

American Society for Quality Control
611 East Wisconsin Avenue
Milwaukee, Wisconsin 53202

Z1.4-1993, Sampling Procedures and Tables for Inspection by Attributes. (This document supersedes MIL-STD-105E).

American Society for Testing and Materials (ASTM)

100 Barr Harbor Drive
West Conshohocken, Pennsylvania 19428-2959

Standard Guide for Integrity Testing of Porous Barrier Medical Packages, ASTM F1585-95.

Standard Terminology Relating to Barrier Materials for Medical Packaging, ASTM F1327-98.

Standard Test Method for Detecting Seal Leaks in Porous Medical Packaging by Dye Penetration, ASTM F1929-98.

Standard Test Method for Determination of Leaks in Flexible Packaging by Bubble Emission, ASTM D3078-94.

Standard Test Method for Determining Integrity of Seals for Medical Packaging by Visual Inspection, ASTM F1886-98.

Standard Test Methods for Failure Resistance of Unrestrained and Nonrigid Packages for Medical Applications, ASTM F1140-96.

Standard Test Method for Leakage Testing of Empty Rigid Containers by Vacuum Method, ASTM D4991-94.

Standard Test Method for Leaks Using Bubble Emission Techniques, ASTM E515-95.

Standard Test Methods for Seal Strength of Flexible Barrier Materials, ASTM F88-94.

Parenteral Drug Association (PDA):
7500 Old Georgetown Road, Suite 620
Bethesda, Maryland 20814

Technical Monograph No. 1, Validation of Steam Sterilization Cycles, 1978

Technical Monograph No. 2, Validation of Aseptic Filling for Solution Drug Products, 1980

Technical Report No. 3, Validation of Dry Heat Processes Used for Sterilization and Depyrogenation, 1981

Health Industry Manufacturers Association (HIMA)
1200 G Street, N.W.
Washington, D.C. 20005

HIMA Reference on Sterile Packaging, (HIMA Publication 93-7) 1993

United States Pharmacopeia the National Formulary, USP 23, NF18 (1995):

U. S. Pharmacopeial Convention, Inc.
12601 Twinbrook Parkway
Rockville, Maryland 20852

- Bacterial Endotoxins Test
- Biological Indicators
- Biological Indicator for Dry-heat Sterilization, Paper Strip
- Biological Indicator for EO Sterilization, Paper Strip
- Biological Indicator for Steam Sterilization, Paper Strip
- Microbial Limit Tests
- Pyrogen Test (USP rabbit test)
- Sterilization and Sterility Assurance of Compendial Articles
- Sterility Tests
- Transfusion and Infusion Assemblies

B. ATTACHMENTS

ATTACHMENT A - CLASS I DEVICES EXEMPT FROM MOST OF THE QS/GMP REQUIREMENTS BY CLASSIFICATION REGULATIONS

ATTACHMENT B - ADVISORY LIST OF DEVICES THAT ARE INTENDED FOR SURGICAL IMPLANT OR SUSTAINING LIFE

ATTACHMENT B-1 - SIGNIFICANT RISK DEVICES

ATTACHMENT C - MODEL WARNING LETTERS **(Revised)**

ATTACHMENT D - DECISION CHART - AUTHORITY TO REVIEW DESIGN CONTROL RECORDS

ATTACHMENT E - SUMMARY OF MDR REPORTING REQUIREMENTS

ATTACHMENT F - SUMMARY OF TRACKING REQUIREMENTS

ATTACHMENT G - SUMMARY OF CORRECTIONS AND REMOVALS REQUIREMENTS

C. PROGRAM CONTACTS

1. ORA Contacts

   a. Questions regarding inspectional requirements and/or technical assistance:

Division of Emergency & Investigational Operations
Medical Device Group
301-827-5645

b. Questions about accessing or connecting to the CDRH Center Information retrieval System (CIRS) call:

CDRH Help Desk
(301) 594-4550, EXT. 104

An easy method for Field Users to access the system is to log on to the regional VAX, then type:

TELNET apps <return>

Field Users should set up their communication program to emulate a VT100 or other option before logging onto the Regional VAX.

c. Questions regarding sampling of devices and laboratory capabilities:

Division of Field Science (DFS), HFC-140
Telephone: (301) 443-3007

d. The WEAC contact points for testing medical devices is:

Laurence Coyne, Ph.D.
Director, Engineering Branch, HFR-NE480
Telephone: (781) 729-5700, ext. 761

Martin J. Finkelson
Director, Analytical Branch, HFR-NE460
Telephone: (781) 729-5700

e. Questions regarding COMSTAT

Gillie Kovalsky
Medical Products Quality Assurance Staff (MPQA), HFC-240
Telephone: (301) 827-0390

2. District Office Contacts For Industry Management Concerns About Their QS/GMP Compliance Status.

Atlanta	Ballard Graham
Baltimore	Elaine Cole
New England	John Marzilli

Buffalo	Edward Thomas
Chicago	Ray Mlecko
Cincinnati	Guy Cartwright
Dallas	Austin Templer
Denver	William Sherer
Detroit	John Dempster
Kansas	Robert Wilson
Los Angeles	Elaine Messa
Minneapolis	James Rahto
Nashville	Ray Hedblad
New Orleans	James Green
New Jersey	Doug Ellsworth
New York	Otto Vitillo
Florida	Timothy Couzins
Philadelphia	Thomas Gardine
San Francisco	Andrea Scott
San Juan	Gordon Cox
Seattle	David Pettenski
St. Louis	Charles Bringman
Foreign Firms	Marje Hoban (CDRH)

3. CDRH Contacts

NOTE: See the CDRH/OC Organizational Structure at the end of Part VI to identify which unit within OC is responsible for answering your question or giving you guidance, depending on the type of device.

a. MDR Regulation Interpretation and Policy Questions:

Reporting Systems Monitoring Branch, HFZ-533
Division of Surveillance Systems, OSB
Telephone: (301) 594-2735

Data retrieval of MDR reports:

Information Analysis Branch, HFZ-531
Division of Surveillance Systems, OSB
Telephone: (301) 827-7537

b. Industry MDR Report: (301) 427-7500. This telephone number should be used to request permission to submit a report by facsimile. Do not call this phone number to make inquiries or to submit a report by telephone.

c. Questions regarding sampling and/or testing of **general medical** devices.

William Regnault

Division of Mechanics and Material Sciences, HFZ-150
Telephone: (301) 827-4748

d. Express Mail Address for All Regulatory Action Recommendations:

Field Programs Branch, HFZ-306
Office of Compliance
Center for Devices and Radiological Health
2094 Gaither Road
Rockville, Maryland 20850

e. Questions regarding the interpretation and applicability of the device Quality System regulation and GMP exemptions:

Kimberly A. Trautman
Quality Systems/GMP Expert, HFZ-340
Telephone: (301) 594-4648 ext.126

or,

Contact the appropriate Division/Branch in the Office of Compliance for the subject device.

f. Questions regarding remanufacturing, refurbishing/reconditioning of used devices:

Wes Morgenstern
Division of Program Operations, HFZ-305
Telephone: (301) 594-4699 ext. 102

g. Questions regarding the reprocessing of single use devices:

Larry Spears
Division of Enforcement III, HFZ-340
Telephone: (301) 594-4646 ext. 153

h. Questions regarding this Compliance Program:

Allen Wynn
Field Programs Branch, HFZ-306
Telephone: (301) 594-4695 ext. 115
Fax: (301) 594-4715

i. Questions regarding compliance of product software, stand alone software, process equipment software or the Year 2000 problem:

Stewart Crumpler

Office of Compliance Software Expert, HFZ-340
Telephone: (301) 594-4659 ext. 119

j. Questions regarding aspects of sterilization technology should be directed to:

Sarah Mowitt
Division of Enforcement I, HFZ-323
Office of Compliance
Telephone: (301) 594-4595

Candace McManus
Division of Enforcement II, HFZ-333
Office of Compliance
Telephone: (301) 594-4618

k. Questions regarding Electronic Records and Electronic signatures of should be directed to:

Christine Nelson
Division of Enforcement II, HFZ-330
Telephone: (301) 594-4611 ext. 134

l. Questions regarding potential or proposed regulatory actions should be directed to the appropriate CDRH/OC Case Expert:

OC Case Experts

Louis Kaufman	(HFZ-320)	(301) 594-4598
Andrea Latish	(HFZ-330)	(301) 594-4611
Karen Stutsman	(HFZ-340)	(301) 594-4646

Device Panel Assignments

Anesthesiology	Karen Stutsman
Cardiovascular	Karen Stutsman
Chemistry	Louis Kaufman
Dental	Andrea Latish
Ear, Nose, and Throat	Andrea Latish
Gastroenterology and Urology	Andrea Latish
General and Plastic Surgery	Louis Kaufman
General Hospital	Andrea Latish
Hematology	Louis Kaufman
Immunology	Louis Kaufman
Microbiology	Louis Kaufman
Neurology	Karen Stutsman
Obstetrics and Gynecology	Karen Stutsman
Ophthalmic	Karen Stutsman
Orthopedics	Karen Stutsman
Pathology	Louis Kaufman
Physical Medicine	Karen Stutsman
Radiology	Louis Kaufman

4. FDA Web Sites:

   a. FDA home page: http://www.fda.gov

   b. ORA home page: http://www.fda.gov/ora/

   c. CDRH home page: http://www.fda.gov/cdrh/

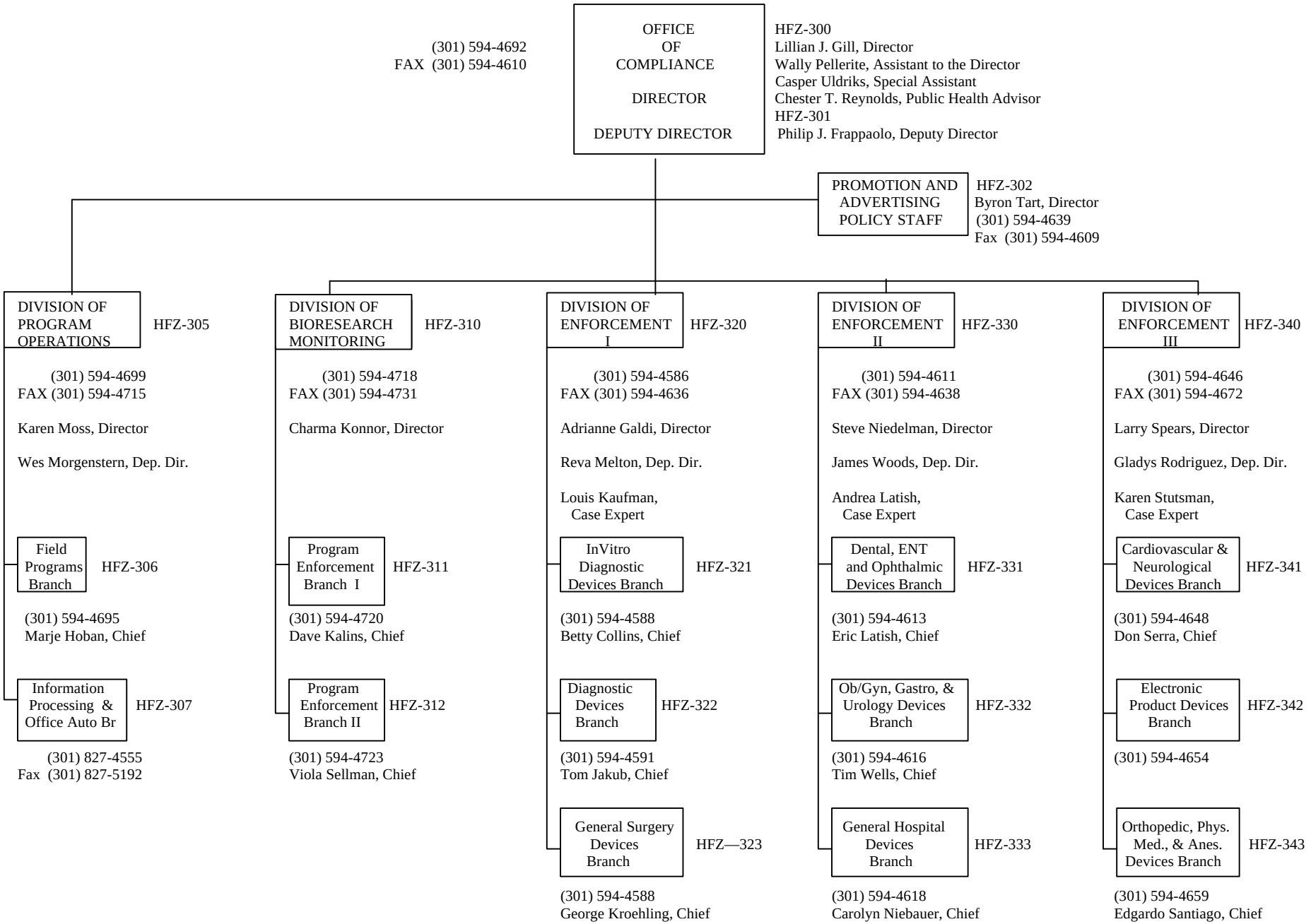
   d. MDR: http://www.fda.gov/cdrh/mdr.html

   e. QSIT Guide: http://www.fda.gov/cdrh/gmp/qsitbook.html

   f. FDA Recognized Standards related to Sterilization of Medical Devices : http://www.fda.gov/cdrh/modact/steril.html

   g. The Biologics and Devices Intercenter Agreement: http://www.fda.gov/oc/ombudsman/bio-dev.htm

OFFICE OF COMPLIANCE ORGANIZATIONAL STRUCTURE



Registration and Listing
(301) 495-7726

ATTACHMENT A

CLASS I DEVICES EXEMPT FROM MOST OF THE QS/GMP REQUIREMENTS BY CLASSIFICATION REGULATIONS

THE FOLLOWING LIST OF EXEMPTED CLASS I DEVICES IS ARRANGED IN PRODUCT CODE SEQUENCE.

TO USE THIS LIST CONSULT THE KEY WORD LIST FOR DEVICES TO DETERMINE THE PRODUCT CODE. THE KEY WORD LIST WAS FORMERLY INCLUDED IN THE EDRO DATA CODES MANUAL (TN-84-1) AND WILL BE ON FILE IN THE DISTRICT'S REFERENCE FILE.

ANESTHESIOLOGY DEVICES

(Final Regulation Published in July 16, 1982 FEDERAL REGISTER;
EFFECTIVE DATE: 8/16/82)

			REGULATION
73	BTB	HOOK, ETHER	868.5420
73	BXJ	CLIP, NOSE	868.6225
73	BXL	ALGESIMETER, MANUAL	868.1030
73	BYN	CHAIR, POSTURE, FOR CARDIAC	868.5365
73	BYO	BOTTLE, BLOW	868.5220
73	BYW	REBREATHING DEVICE	868.5675
73	BZN	CART, EMERGENCY, CARDIOPULMONARY	868.6175
73	CBG	SPREADER, CUFF	868.5760
77	EPE	BRUSH, CLEANING, TRACHEAL TUBE	868.5795
73	JFE	VALVE, SWITCHING (PLOSS)	868.1965

CARDIOVASCULAR

74	---	(No devices have been exempted)

CLINICAL CHEMISTRY DEVICES

(Final Regulation Published in May 1, 1987 FEDERAL REGISTER;
EFFECTIVE DATE: 7/30/87)

75	JBS	TIMER, GENERAL LABORATORY	862.2050
75	JJP	ION SELECTIVE ELECTRODES (NON-SPECIFIED)	862.2050
75	JQO	ANALYTICAL BALANCE	862.2050
75	JQQ	DIALYZER	862.2050
75	JQY	PH METER	862.2050
75	JQZ	POLARIMETER	862.2050
75	JRB	MICRO MIXER	862.2050
75	JRG	HEATING BLOCK	862.2050
75	JRJ	DRYING UNIT	862.2050
75	JRK	EVAPORATOR	862.2050
75	JRL	MEMBRANE FILTER UNIT	862.2050
75	JRM	FREEZER	862.2050
75	JRO	BLENDER/MIXER	862.2050

75	JRQ	SHAKER/STIRRER	862.2050
75	JRR	TEMPERATURE REGULATOR	862.2050

DENTAL DEVICES

(Final Regulation Published in August 12, 1987 FEDERAL REGISTER;
EFFECTIVE DATE: 9/11/87)

76	EBH	MATERIAL IMPRESSION TRAY RESIN	872.3670
76	EEA	BASE PLATE SHELLAC	872.6200
76	EEJ	GUARD, DISK	872.6010
76	EFH	PAPER, ARTICULATION	872.6140
76	EFW	TOOTH BRUSH, MANUAL	872.6855
76	EFX	PROTECTOR, SILICATE	872.6670
76	EGD	INTRAORAL DENTAL WAX	872.6890
76	EGZ	FILM, X-RAY HOLDER	872.1905
76	EHJ	DISK, ABRASIVE	872.6010
76	EHK	PROPHYLAXIS CUP	872.6290
76	EHL	POINT, ABRASIVE	872.6010
76	EHM	STRIP, POLISHING AGENT	872.6010
76	EHY	TRAY, IMPRESSION, PREFORMED	872.6880
76	EIE	DAM, RUBBER AND ACCESSORIES	872.6300
76	EJP	ARTICULATOR	872.3150
76	EJQ	WHEEL, POLISHING AGENT	872.6010
76	JET	PICK, MASSAGING	872.6650
76	KCO	TUBE IMPRESSION AND MATRIX	872.5220
76	KCR	FACE BOW	872.3220
76	KCS	PANTOGRAPH	872.3730
76	KHR	SALIVA ABSORBER PAPER	872.6050
76	KMT	DISPOSABLE FLUORIDE TRAY	872.6870
76	KXR	RESIN APPLICATOR	872.4565

EAR, NOSE, AND THROAT DEVICES

(Final Regulation Published in November 6, 1986 FEDERAL REGISTER;
EFFECTIVE DATE: 12/8/86)

77	ESE	LARYNX, ARTIFICIAL (BATTERY-POWERED)	874.3375
77	ETM	GUSTOMETER	874.1500
77	JPN	MANUAL NEBULIZER PUMP	874.5220
77	JXS	BLOCK, CUTTING, ENT	874.3540
77	JXT	CRIMPER, WIRE, ENT	874.3540
77	JXW	DIE, WIRE BENDING, ENT	874.3540
77	JXX	FORCEPS WIRE CLOSURE, ENT	874.3540
77	JXY	JIG, PISTON CUTTING, ENT	874.3540
77	JXZ	PUNCH, GELFOAM	874.3540
77	JYA	SCISSORS, WIRE CUTTING, ENT	874.3540
77	JYB	VISE, OSSICULAR FINGER	874.3540
77	KCL	BLOWER, POWDER, ENT	874.5220

77	KCM	DROPPER, ENT	874.5220
77	KCN	EAR WICK	874.5220
77	KCO	INHALER, NASAL	874.5220

GASTROENTEROLOGY-UROLOGY DEVICES

(Final Regulation Published in November 23, 1983 Federal Register;
EFFECTIVE DATE: 12/23/83)

78	EXI	PASTE-ON DEVICE FOR INCONTINENCE	876.5250
78	EXJ	DEVICE, INCONTINENCE, UROSHEATH TYPE	876.5250
78	EXN	HERNIA SUPPORT	876.5970
78	EYQ	PROTECTIVE GARMENT FOR INCONTINENCE	876.5920
78	EYT	SHEATH, CORRUGATED RUBBER	876.5250
78	FAQ	BAG, LEG (FOR EXTERNAL USE)	876.5250
78	FCE	ENEMA KIT	876.5210
78	FFH	COLLECTOR, URINE, PEDIATRIC	876.5250
78	KNX	URINE COLLECTOR AND ACCESSORIES (not intended to be connected to an indwelling catheter:	876.5250

GENERAL AND PLASTIC SURGERY DEVICES

79	KCZ	PROSTHESIS, BREAST, EXTERNAL	878.3800

GENERAL HOSPITAL AND PERSONAL USE DEVICES

(Final Regulation Published in October 21, 1980 Federal Register:
EFFECTIVE DATE: 11/20/80)

80	FLH	SANITIZER, MECHANICAL	880.6800
80	FMA	DEPRESSOR, TONGUE	880.6230
80	FME	GOWN, EXAMINATION	880.6265
80	FMF	NON-STERILE IRRIGATING SYRINGE (SYRINGE)	880.5860
80	FMH	CONTAINER, SPECIMEN	880.6175
80	FML	CHAIR, BLOOD DONOR (NON-WHEELED)	880.6140
80	FMP	PROTECTOR, SKIN PRESSURE	880.6450
80	FMQ	RESTRAINT PROTECTIVE	880.6760
80	FMR	TRANSFER DEVICE, PATIENT, MANUAL	880.6785
80	FMW	MATTRESS COVER (FOR MEDICAL PURPOSE)	880.6190
80	FNJ	BED, MANUAL	880.5120
80	FNN	NIPPLE, LAMBS FEEDING	880.5640
80	FNP	URINAL	880.6730
80	FNS	RING CUTTER	880.6200
80	FNY	BASIN, EMESIS	880.6730
80	FOA	BOARD, CARDIOPULMONARY	880.6080
80	FOB	BEDPAN	880.6730
80	FOK	PAD, NEONATAL EYE	880.6025
80	FOR	NON-STERILE ABSORBENT TIPPED APPLICATOR	880.5270

80	FPF	BOTTLE, HOT/COLD WATER	880.6085
80	FPP	STRETCHER, HAND CARRIED	880.6900
80	FPS	BOARD, BED	880.6070
80	FQA	SCALE, SURGICAL SPONGE	880.2740
80	FQJ	THERAPEUTIC SCROTAL SUPPORT	880.5820
80	FQK	BINDER, PERINEAL	880.5160
80	FQL	STOCKING, MEDICAL SUPPORT	880.5780
80	FQM	BANDAGE, ELASTIC	880.5075
80	FRI	SCALE, STAND-ON, PATIENT	880.2700
80	FRJ	CHAIR, GERIATRIC (NON-WHEELED, NON-POWERED)	880.6140
80	FRK	CHAIR, EXAMINATION, AND TREATMENT	880.6140
80	FRL	MEDICAL ABSORBENT FIBER	880.5300
80	FRP	PEDIATRIC POSITION HOLDER	880.5680
80	FSD	BINDER, ABDOMINAL	880.5160
80	FSL	STRETCHER, HAND CARRIED	880.6900
80	IKY	NON-POWERED FLOTATION THERAPY MATTRESS	880.5150
80	KIA	COVER, CAST	880.6185
80	KME	MEDICAL DISPOSABLE BEDDING	880.6060
80	KMO	BINDER, ELASTIC	880.5160
80	KYR	BAG, ICE	880.6050
80	KYT	BATTERY POWERED EXAM LIGHT	880.6350
80	KYW	GRADUATED LIQUID MEDICATION	880.6430
80	KYX	LIQUID MEDICATION DISPENSER	880.6430
80	LBJ	VEIN STABILIZATION DEVICE	880.6980

IMMUNOLOGY DEVICES

82	---	(No devices have been exempted)	

MICROBIOLOGY DEVICES

(Final Regulation Published in November 9, l982 FEDERAL REGISTER;
EFFECTIVE DATE: 12/9/82)

83	GMB	LIGHT, WOOD'S FLUORESCENCE	866.2600
83	JTB	MEDIA DISPENSING/STACKING DEVICES	866.2440
83	JTM	ANAEROBIC GLOVE BOX	866.2120
83	JTQ	INCUBATORS/WATER BATHS, ALL	866.2540
83	KZC	MANUAL COLONY COUNTER	866.2180

NEUROLOGY DEVICES

(Final Regulation Published in September 4, 1979 FEDERAL REGISTER;
EFFECTIVE DATE: 10/4/79)

84	GWI	TWO POINT DISCRIMINATOR	882.1200
84	GWX	TUNING FORK	882.1525
84	GWZ	PERCUSSOR	882.1700
84	GXB	ESTHESIOMETER	882.1500

OBSTETRICAL/GYNECOLOGICAL

85	---	(No devices have been exempted)	

OPHTHALMIC DEVICES

(Final Regulation Published in September 2, 1987 FEDERAL REGISTER;
EFFECTIVE DATE: 10/2/87)

86	HIT	TESTER, COLOR VISION	886.1170
86	HJC	OCULAR ESTHESIOMETER	886.1040
86	HJF	MAGNIFIER, HAND-HELD, LOW-VISION	886.5540
86	HJH	BINOCULAR LOUPE, LOW POWER	886.5120
86	HJI	LENS, FUNDUS, HRUBY, DIAGNOSTIC	886.1395
86	HJJ	LENS, FRESNEL, FLEXIBLE, DIAGNOSTIC	886.1390
86	HJL	LENS, CONDENSING, DIAGNOSTIC	886.1380
86	HKB	TELESCOPE, HAND-HELD, LOW-VISION	886.5870
86	HKC	SPECTACLE MICROSCOPE, LOW-VISION	886.5540
86	HKD	TAPE, NYSTAGMUS	886.1905
86	HKF	MIRROR, HEADBAND, OPHTHALMIC	886.1500
86	HKG	FORNISXCOPE	886.1320
86	HKK	TELESCOPE, SPECTACLE, LOW-VISION	886.5870
86	HKM	RETINOSCOPE, BATTERY-POWERED	886.1780
86	HKN	REFRACTOR, MANUAL, NON-POWERED,	886.1770
86	HKQ	PRISM, ROTARY, OPHTHALMIC	886.1665
86	HKR	LENS, MADDOX	886.1400
86	HKT	PRISM, FRESNEL, OPHTHALMIC	886.1655
86	HKW	PRISM, BAR, OPHTHALMIC	886.1650
86	HLC	INSTRUMENT, MEASURING, STEREOPSIS	886.1460
86	HLE	RULER, NEAR POINT (PUNCTOMETER)	886.1790
86	HLH	PUPILLOMETER, MANUAL	886.1700
86	HLJ	OPHTHALMOSCOPE BATTERY-POWERED	886.1570
86	HLK	SCREEN, TANGENT, TARGET BATTERY-POWERED	886.1810
86	HLN	GAUGE, LENS, OPHTHALMIC	886.1420
86	HLO	TEST, SPECTACLE DISSOCIATION, BATTERY-POWERED	886.1910
86	HLP	TARGET, FUSION AND STEREOSCOPIC	886.1880
86	HLR	KERATOSCOPE, BATTERY-POWERED	886.1350
86	HMD	CHAIR, OPHTHALMIC, MANUAL	886.1140
86	HMG	STAND, INSTRUMENT, OPHTHALMIC	886.1860
86	HMJ	SCREEN, TANGENT, PROJECTION BATTERY-POWERED	886.1810
86	HMM	DISTOMETER	886.1190
86	HMQ	MARKER, SCLERA	886.4570
86	HMR	MARKER, OCULAR	886.4570
86	HMS	DRUM, OPHTHALMIC KNIFE TEST	886.4230
86	HMX	CANNULA, OPHTHALMIC	886.4350
86	HMZ	TRABECULOTOME	886.4350

86	HNA	SPUD, OPHTHALMIC	886.4350
86	HNB	SPOON, OPHTHALMIC	886.4350
86	HNC	SPECULA, OPHTHALMIC	886.4350
86	HND	SPATULA, OPHTHALMIC	886.4350
86	HNE	SNARE, ENUCLEATING	886.4350
86	HNF	SCISSORS, OPHTHALMIC	886.4350
86	HNG	RONGEUR, LACHRYMAL SAC	886.4350
86	HNH	RING, OPHTHALMIC (FLIERINGA)	886.4350
86	HNI	RETRACTOR, OPHTHALMIC	886.4350
86	HNJ	PUNCH, CORNEO-SCLERAL	886.4350
86	HNK	PROBE, TRABECULOTOMY	886.4350
86	HNL	PROBE, LACHRYMAL	886.4350
86	HNM	NEEDLE, OPHTHALMIC SUTURING	886.4350
86	HNN	KNIFE, OPHTHALMIC	886.4350
86	HNP	INTRODUCER, SPHERE	886.4350
86	HNQ	HOOK, OPHTHALMIC	886.4350
86	HNR	FORCEPS, OPHTHALMIC	886.4350
86	HNS	EXPRESSOR	886.4350
86	HNT	ERISOPHAKE	886.4350
86	HNW	DILATOR, LACHRYMAL	886.4350
86	HNX	DEPRESSOR, ORBITAL	886.4350
86	HNY	CYSTOTOME	886.4350
86	HNZ	CURETTE, OPHTHALMIC	886.4350
86	HOA	COMPRESSOR, ORBITAL	886.4350
86	HOB	CLAMP, MUSCLE, OPHTHALMIC	886.4350
86	HOC	CLIP, IRIS RETRACTOR	886.4350
86	HOD	CLAMP, EYELID, OPHTHALMIC	886.4350
86	HOE	CALIPER, OPHTHALMIC	886.4350
86	HOF	BURR, CORNEAL, MANUAL	886.4350
86	HOH	SPECTACLE, OPERATING (LOUPE), OPHTHALMIC	886.4770
86	HOI	SPECTACLE, MAGNIFYING	886.5840
86	HOJ	SCREEN, TANGENT, TARGET	886.1810
86	HOL	SCREEN, TANGENT, FELT (CAMPIMETER)	886.1810
86	HON	PERIMETER, MANUAL	886.1605
86	HOP	CAMPIMETER, STEREO, BATTERY-POWERED	886.1810
86	HOQ	GRID, AMSLER	886.1330
86	HOR	SIMULITAN (INCLUDING CROSSED CYLINDER)	886.1840
86	HOT	AID, VISION, IMAGE-INTENSIFICATION, BATTERY-POWERED	886.5910
86	HOW	DRUM, OPTOKINETIC	886.1200
86	HOX	CHART, VISUAL ACUITY	886.1150
86	HOY	SHIELD, EYE, OPHTHALMIC	886.4750
86	HPA	FRAME, TRIAL, OPHTHALMIC	886.1415
86	HPB	CLIP, LENS, TRIAL, OPHTHALMIC	886.1410
86	HPD	LENS, BAGOLINI	886.1375
86	HPE	AID, VISION, OPTICAL, BATTERY-POWERED	886.5915
86	HPN	MAGNET, PERMANENT	886.4445
86	HRH	TREPHINE, MANUAL, OPHTHALMIC	886.4350
86	HRK	TABLE, INSTRUMENT, MANUAL, OPHTHALMIC	886.4855

ORTHOPEDIC DEVICES

(Final Regulation Published in September 4, 1987 FEDERAL REGISTER;
EFFECTIVE DATE: 10/5/87)

87	HST	APPARATUS, TRACTION, NON-POWERED ORTHOPEDIC	888.5850
87	JQZ	TRACTION COMPONENT, NON-INVASIVE	862.2050
87	LGF	CAST COMPONENT	888.5940
87	LGG	MANUAL CAST APPLICATION AND REMOVAL INSTRUMENT	888.5980

HEMATOLOGY AND PATHOLOGY DEVICES

(Final Regulation Published in September 12, 1980 FEDERAL REGISTER;
EFFECTIVE DATE: 10/14/80)

88	GFL	PONCEAU STAIN	864.1850
88	GFR	NEW METHYLENE BLUE STAIN	864.1850
88	GGD	CRYSTAL VIOLET FOR HEMATOLOGY	864.1850
88	GGH	IRON STAINS	864.1850
88	GGI	PERIODIC ACID SCHIFF STAIN	864.1850
88	GHP	BRILLIANT CRESYL BLUE	864.1850
88	GIX	TOLUIDINE BLUE	864.1850
88	GJH	RETICULOCYTE STAIN	864.1850
88	GJJ	HEINZ BODY STAINS	864.1850
88	GJL	ROMANOWSKY STAINS	864.1850
88	GJO	SLIDES AND COVERSLIPS	864.3010
88	GJY	MICROSCOPE	864.3600
88	GLP	GIEMSA STAIN	864.1850
88	HYB	EOSIN Y	864.1850
88	HYC	FAST GREEN	864.1850
88	HYD	FAST RED SALT B	864.1850
88	HYE	FONTANNA SILVER SOLUTION	864.1850
88	HYH	GOLD CHLORIDE	864.1850
88	HYI	GRAMS IODINE	864.1850
88	HYJ	HEMATOXYLIN	864.1850
88	HYK	HEMATOXYLIN HARRIS'S	864.1850
88	HYL	HEMATOXYLIN MAYER'S	864.1850
88	HYO	HEMATOXYLIN WEIGERT'S	864.1850
88	HYQ	IRON CHLORIDE-WEIGERT	864.1850
88	HYR	LEUCO-PATENT BLUE	864.1850
88	HYS	LIGHT GREEN	864.1850
88	HYW	MALLORY'S TRICHROME STAIN	864.1850
88	HYY	METANIL YELLOW	864.1850
88	HYZ	METHENAMINE SILVER	864.1850
88	HZA	METHYL GREEN	864.1850
88	HZC	MUCICARMINE	864.1850
88	HZD	MULLER'S COLLOIDAL IRON	864.1850

88	HZE	NILE BLUE	864.1850
88	HZF	NUCLEAR FAST RED	864.1850
88	HZG	OIL RED O	864.1850
88	HZH	ORANGE G	864.1850
88	HZJ	PAPANICOLAOU STAIN	864.1850
88	HZL	PHLOXINE B	864.1850
88	HZM	PHOSPHOTUNGSTIC ACID HEMATOXYLIN	864.1850
88	HZN	PICRO METHYL BLUE	864.1850
88	HZO	PONCEAU STAIN	864.1850
88	HZP	PYRONIN	864.1850
88	HZQ	RED VIOLET - LB	864.1850
88	HZR	RESORCIN FUCHSIN	864.1850
88	HZS	SAFRANIN	864.1850
88	HZT	SCHIFF REAGENT	864.1850
88	HZX	SILVER NITRATE	864.1850
88	HZY	SIRIUS RED	864.1850
88	HZZ	SUDAN BLACK B	864.1850
88	IAA	TITAN YELLOW	864.1850
88	IAB	TOLUIDINE BLUE	864.1850
88	IAC	VAN GIESON'S STAIN	864.1850
88	IAD	VAN GIESON'S PICRO-FUCHSIN	864.1850
88	IAE	WEIGERT'S IRON HEMATOXYLIN	864.1850
88	IAF	WRIGHT'S STAIN	864.1850
88	IAM	LUGOL'S SOLUTION	864.4010
88	IAT	APATHY'S GUM SYRUP	864.4010
88	IAW	COLLODION	864.4010
88	IBJ	ICROSCOPE, LIGHT	864.3600
88	IBK	MICROSCOPE, FLUORESCENCE/UV	864.3600
88	IBL	MICROSCOPE, INVERTED STAGE, TISSUE CULTURE	864.3600
88	IBM	MICROSCOPE, PHASE CONTRAST	864.3600
88	ICC	EOSIN B	864.1850
88	ICD	DARROW RED	864.1850
88	ICF	CRYSTAL VIOLET FOR HISTOLOGY	864.1850
88	ICG	CRESYL VIOLET ACETATE	864.1850
88	ICH	CONGO RED	864.1850
88	ICI	CHROME ALUM HEMATOXYLIN	864.1850
88	ICL	CARBOL FUCHSIN	864.1850
88	ICM	BRILLIANT YELLOW	864.1850
88	ICN	BIEBRICH SCARLET	864.1850
88	ICO	BEST'S CARMINE	864.1850
88	ICQ	AZURE A	864.1850
88	ICR	AZOCARMINE B	864.1850
88	ICS	AZOCARMINE G	864.1850
88	ICT	AZAN COUNTERSTAIN	864.1850
88	ICX	ANILINE	864.1850
88	ICY	ANILINE ACID FUCHSIN	864.1850
88	ICZ	AMMONIACAL SILVER HYDROXIDE SILVER NITRATE	864.1850
88	IDA	ALCIAN BLUE	864.1850

88	IDB	ALDEHYDE FUCHSIN	864.1850
88	IDC	ACRIDINE ORANGE	864.1850
88	IDD	ALIZARIN RED	864.1850
88	IDE	ACID HEMATEIN	864.1850
88	IDF	ACID FUCHSIN	864.1850
88	IDL	MICROTOME, ACCESSORIES	864.3010
88	IDM	MICROTOME, ULTRA	864.3010
88	IDN	MICROTOME, FREEZING ATTACHMENT	864.3010
88	IDO	MICROTOME, ROTARY	864.3010
88	IDP	MICROTOME, CRYOSTAT	864.3010
88	IDQ	INFILTRATOR	864.3010
88	IDR	OVENS, PARAFFIN	864.3010
88	IDS	MELTING POT, PARAFFIN	864.3010
88	IDT	MELTING POINT APPARATUS, PARAFFIN	864.3010
88	IDW	DISPENSERS, PARAFFIN	864.3010
88	IDX	SIEVES, TISSUE	864.3010
88	IDY	FLOTATION BATHS, TISSUE	864.3010
88	IDZ	CASSETTES, TISSUE	864.3010
88	IEG	TABLE, SLIDE WARMING	864.3010
88	IEH	LAMPS, SLIDE WARMING	864.3010
88	IER	OLYETHYLENE GLYCOL (CARBOWAX)	864.4010
88	IEX	GELATIN	864.4010
88	IEZ	CELLOIDIN	864.4010
88	IFF	DECALCIFIER SOLUTION, ELECTROLYTIC	864.4010
88	IFH	ZENKER'S SOLUTION	864.4010
88	IFI	SPRAYS, SYNTHETIC, SMEAR	864.4010
88	IFJ	RICHARDSON GLYCOL FIXATIVE	864.4010
88	IFL	POLETHYLENE GLYCOL PRESERVATIVE	864.4010
88	IFN	ORTH'S SOLUTION	864.4010
88	IFO	NEWCOMER'S SOLUTION	864.4010
88	IFP	FORMALIN, NEUTRAL BUFFERED	864.4010
88	IFQ	MERCURIC CHLORIDE FORMULATIONS	864.4010
88	IFS	HELLY SOLUTION	864.4010
88	IFZ	GELATIN FOR SPECIMEN ADHESION	864.4010
88	IGB	FORMALIN-SODIUM ACETATE SOLUTION	864.4010
88	IGC	FORMALIN-SALINE	864.4010
88	IGD	FORMOL CALCIUM SOLUTION	864.4010
88	IGE	FORMALIN AMMONIUM BROMIDE	864.4010
88	IGF	FORMALIN-ALCOHOL-ACETIC ACID	864.4010
88	IGG	FORMALDHYDE (FORMALIN, FORMOL)	864.4010
88	IGK	CLARKE'S SOLUTION	864.4010
88	IGM	CARNOY'S SOLUTION	864.4010
88	IGN	BOUIN'S FLUID	864.4010
88	IHJ	BLENDORS FOR SPUTUM	864.3010
88	IJZ	CLEARING OIL	864.4010
88	JCC	PH BUFFERS	864.4010
88	JCE	ISOTONIC SOLUTION	864.4010
88	JCH	ESTERASE	864.1850
88	JCI	ACID PHOSPHATASE, CYTOCHEMICAL	864.1850
88	JTS	STAINS, MICROBIOLOGIC, ALL	864.1850

88	KDX	DECALCIFIER SOLUTION, ACID CONTAINING	864.4010
88	KDY	CHELATING AGENTS FOR DECALIFICATION	864.4010
88	KDZ	DEALCIFIER DEVICES, ELECTROLYTIC	864.3010
88	KEE	OSMIUM TETROXIDE	864.4010
88	KEF	PARAFORMALDEHYDE	864.4010
88	KEG	LAMPS, MICROSCOPE	864.4010
88	KEH	MICROMETERS, MICROSCOPE	864.3600
88	KEI	CONDENSERS, MICROSCOPE	864.3600
88	KEJ	STAGES, MICROSCOPE	864.3600
88	KEL	ALBUMIN-BASED ADHESIVES	864.4010
88	KEM	CLEARING AGENTS	864.4010
88	KEO	PARAFFIN, ALL FORMULATIONS	864.4010
88	KEP	OIL SOLUBLE MOUNTING MEDIA	864.4010
88	KEQ	WATER SOLUBLE MOUNTING MEDIA	864.4010
88	KER	EMBEDDING CONTAINER	864.3010
88	KES	COVERSLIPS, MICROSCOPE SLIDE	864.3010
88	KET	FILTER, CELL COLLECTION, TISSUE	864.3010
88	KEW	SLIDES, MICROSCOPE	864.3010
88	KFC	METHYLENE BLUE, TISSUE STAIN	864.1850
88	KFD	ANILINE BLUE	864.1850
88	KFE	NEUTRAL RED	864.1850
88	KFL	MICROTOME, SLIDING	864.3010
88	KIY	CHAMBER, SLIDE CULTURE	864.2240
88	KIZ	DISH, TISSUE CULTURE	864.2240
88	KJA	FLASK, TISSUE CULTURE	864.2240
88	KJB	ROLLER APPARATUS	864.2240
88	KJC	ROLLER BOTTLE, TISSUE CULTURE	864.2240
88	KJD	SPINNER FLASK	864.2240
88	KJE	SPINNER SYSTEM, CELL CULTURE	864.2240
88	KJF	SUSPENSION SYSTEM, CELL CULTURE	864.2240
88	KJG	TUBE, TISSUE CULTURE	864.3010
88	KJH	PERFUSION APPARATUS	864.2240
88	KJK	AURAMINE O	864.1850
88	KJL	AZURE C	864.1850
88	KJM	BISMARCK BROWN Y	864.1850
88	KJN	BRILLIANT CRESYL BLUE	864.1850
88	KJO	BRILLIANT GREEN	864.1850
88	KJP	CARMINE	864.1850
88	KJQ	CHLORAZOL BLACK E	864.1850
88	KJR	ERYTHROSIN B	864.1850
88	KJS	ETHYL EOSIN	864.1850
88	KJT	INDIGOCARMINE	864.1850
88	KJW	JANUS GREEN B	864.1850
88	KJX	JENNER STAIN	864.1850
88	KJY	MALACHITE GREEN	864.1850
88	KJZ	MARTIUS YELLOW	864.1850
88	KKA	METHYL ORANGE	864.1850
88	KKB	METHYL VIOLET 2B	864.1850
88	KKC	METHYLENE VIOLET	864.1850
88	KKD	NIGROSIN	864.1850

88	KKE	ORANGE II	864.1850
88	KKF	ORCEIN	864.1850
88	KKG	PROTARGOL S	864.1850
88	KKH	RESAUZRIN TABLET	864.1850
88	KKI	ROSE BENGAL	864.1850
88	KKJ	SUDAN III	864.1850
88	KKK	SUDAN IV	864.1850
88	KKL	THIONIN	864.1850
88	KKM	METHYLENE BLUE THIOCYANATE	864.1850
88	KKP	SILVER CARBONATE SOLUTION	864.1850
88	KKQ	SODIUM PERIODATE	864.1850
88	KKR	POTASSIUM PERIODATE	864.1850
88	KKS	PERIODIC ACID	864.1850
88	KKT	HEMATOXYLIN EHRLICH'S	864.1850
88	KKW	BASIC FUCHSIN	864.1850
88	KQD	HEMATOLOGY STAINS	864.4010

PHYSICAL MEDICINE DEVICES

(Final Regulation Published in November 23, 1983 Federal Register;
EFFECTIVE DATE: 12/23/83)

89	IKW	UTENSIL, HOMEMAKING	890.5050
89	IKX	AID, TRANSFER	890.5050
89	ILC	UTENSIL, EATING	890.5050
89	ILD	ADAPTOR, DRESSING	890.5050
89	ILE	SLING, ARM, OVERHEAD SUPPORTED	890.3475
89	ILG	STOCKING, ELASTIC	890.3475
89	ILH	SPLINT, HAND, AND COMPONENTS	890.3475
89	ILI	SLING, ARM	890.3640
89	ILP	SYSTEM, COMMUNICATION, NON-POWERED	890.3700
89	ILS	ADAPTOR, HYGIENE	890.5050
89	ILT	ADAPTOR, RECREATIONAL	890.5050
89	ILW	ADAPTOR, GROOMING	890.5050
89	ILZ	ACCESSORIES, TRACTION	890.5925
89	IMA	HEAT PACK, MOIST	890.5730
89	IME	PACK, HOT OR COLD, REUSABLE	890.5700
89	IMS	SUPPORT, HEAD AND TRUNK, WHEELCHAIR	890.3910
89	IMX	BOARD, LAP, WHEELCHAIR	890.3910
89	IMY	ARMBOARD, WHEELCHAIR	890.3910
89	IMZ	HOLDER, CRUTCH AND CANE, WHEELCHAIR	890.3910
89	INC	CUFF, PUSHER, WHEELCHAIR	890.3910
89	INE	SLING, OVERHEAD SUSPENSION, WHEELCHAIR	890.3910
89	INF	SCALE, PLATFORM, WHEELCHAIR	890.3940
89	INP	TIPS AND PADS, CANE, CRUTCH AND WALKER	890.3790
89	INT	PLINTH	890.3520
89	IOD	COMPONENTS, EXERCISE	890.5350
89	IOE	BARS, PARALLEL, EXERCISE	890.5370
89	IOG	TREADMILL, MECHANICAL	890.5370
89	ION	EXERCISER, NON-MEASURING	890.5370

89	IOY	SUPPORT, ARM	890.3475
89	IOZ	SPLINT, ABDUCTION, CONGENITAL HIP DISLOCATION	890.3665
89	IPG	SHOE, CAST	890.3025
89	IPM	COVER, LIMB	890.3025
89	IPR	CRUTCH	890.3150
89	IPS	CANE	890.3075
89	IPT	ORTHOSIS, THORACIC	890.3490
89	IPW	ORTHOSIS, SACROILIAC, SOFT	890.3490
89	IPX	ORTHOSIS, RIB FRACTURE, SOFT	890.3490
89	IPY	ORTHOSIS, LUMBO-SACRAL	890.3490
89	IQE	ORTHOSIS, LUMBAR	890.3490
89	IQF	ORTHOSIS, CERVICAL-THORACIC, RIGID	890.3490
89	IQG	ADAPTOR, HOLDER, SYRINGE	890.5050
89	IQI	ORTHOSIS, LIMB BRACE	890.3475
89	IQJ	SPLINT, CLAVICLE	890.3490
89	IQK	ORTHOSIS, CERVICLE	890.3490
89	IQM	SPLINT, TEMPORARY, TRAINING	890.3025
89	IQO	DEVICE, PROSTHESIS ALIGNMENT	890.3025
89	IQP	ROTATOR, TRANSVERSE	890.3025
89	IQQ	JOINT, SHOULDER, EXTERNAL LIMB COMPONENT	890.3420
89	IQW	HOOK, EXTERNAL LIMB COMPONENT, POWERED	890.3420
89	IQX	HOOK, EXTERNAL LIMB COMPONENT, MECHANICAL	890.3420
89	IQZ	HAND, EXTERNAL LIMB COMPONENT, POWERED	890.3420
89	IRA	HAND, EXTERNAL LIMB COMPONENT, MECHANICAL	890.3420
89	IRD	JOINT, ELBOW, EXTERNAL LIMB COMPONENT, MECHANICAL	890.3420
89	IRE	JOINT, ELBOW, EXTERNAL LIMB COMPONENT, POWERED	890.3420
89	ISH	ANKLE/FOOT, EXTERNAL LIMB COMPONENT	890.3420
89	ISL	JOINT, HIP, EXTERNAL LIMB COMPONENT	890.3420
89	ISM	PYLON, POST SURGICAL	890.3025
89	ISN	CABLE	890.3420
89	ISP	VALVE, PROSTHESIS	890.3420
89	ISR	BAND OR BELT, PELVIC SUPPORT	890.3425
89	ISS	PROSTHESIS, THIGH SOCKET, EXTERNAL COMPONENT	890.3420
89	ISY	JOINT, KNEE, EXTERNAL LIMB COMPONENT	890.3420
89	ISZ	UNIT, WRIST, EXTERNAL LIMB COMPONENT, MECHANICAL	890.3420
89	ITC	STIRRUP, EXTERNAL BRACE COMPONENT	890.3410
89	ITG	BANDAGE, CAST	890.3025
89	ITJ	WALKER, MECHANICAL	890.3825
89	ITM	CAGE, KNEE	890.3475
89	ITN	SPLINT, DENIS BROWN	890.3675
89	ITO	TWISTER, BRACE SETTING	890.3410
89	ITQ	JOINT, KNEE, EXTERNAL BRACE	890.3475
89	ITS	JOINT, HIP, EXTERNAL BRACE	890.3475
89	ITW	JOINT, ANKLE, EXTERNAL BRACE	890.3475
89	KGH	UNIT, WRIST, EXTERNAL LIMB COMPONENT,	890.3420

		POWERED	
89	KHY	CANE, SAFETY WALK	890.3075
89	KND	ACCESSORIES, WHEELCHAIR	884.5390
89	KNL	BOARD, SCOOTER, PRONE	890.5370
89	KNP	ORTHOSIS, CORRECTIVE SHOE	890.3475
89	KTZ	BATH, SITZ, NON-POWERED	888.4150

RADIOLOGICAL DEVICES

(Final Regulation Published in January 20, 1988 FEDERAL REGISTER; EFFECTIVE DATE: 2/19/88)

90	IWY	HOLDER, HEAD, RADIOGRAPHIC	892.1920
90	IXF	TEST PATTERN, RADIOGRAPHIC	892.1940
90	IXG	PHANTOM, ANTHROPOMORPHIC, RADIOGRAPHIC	892.1950

CLINICAL TOXICOLOGY DEVICES

(Final Regulation Published in May 1, 1987 FEDERAL REGISTER; EFFECTIVE DATE: 7/30/87)

91	DJS	UV LIGHT, TLC	862.2270
91	DKK	DEVELOPING TANKS, TLC	862.2270
91	DLC	ATOMIZER, TLC	862.2270
91	DPA	THIN LAYER CHROMATOGRAPHY, APPARATUS, GENERAL USE	862.2270

ATTACHMENT B

ADVISORY LIST OF DEVICES

THAT ARE INTENDED FOR SURGICAL IMPLANT OR SUSTAINING LIFE

ANESTHESIOLOGY DEVICES Page 2

CARDIOVASCULAR DEVICES Page 3

DENTAL DEVICES Page 6

EAR, NOSE, AND THROAT DEVICES Page 6

GASTROENTEROLOGY-UROLOGY DEVICES Page 6

GENERAL AND PLASTIC SURGERY DEVICES Page 8

GENERAL HOSPITAL AND PERSONAL USE DEVICES Page 8

NEUROLOGICAL DEVICES Page 9

OBSTETRICAL AND GYNECOLOGICAL DEVICES Page 11

OPHTHALMIC DEVICES Page 11

ORTHOPEDIC DEVICES Page 11

*SUPPLEMENTAL INFORMATION (#)

Dialysis Systems & Accessories

Peritoneal Dialysis Systems and Accessories Page 17

Hemodialysis Systems and Accessories Page 18

NOTE: The Quality System Regulation no longer refers to critical devices. However, 21 CFR 820.65 requires traceability for all devices that meet the same definition as devices on the Advisory List of Critical Devices - 1988.

PART 868 -- ANESTHESIOLOGY DEVICES

	CFR or FR Cite	Classification Name of Device	Device No. on Original List	Former device name, or Additional Information
1.	868.1200	Indwelling blood oxygen partial pressure (P_{02}) analyzer.	5	Analyzer, oxygen, Neonatal Invasive
2.	868.2375	Breathing frequency monitor.	--	Apnea monitor.
3.	868.5090	Emergency airway needle.	43	Needle, emergency airway.
4.	868.5160(a)	Gas machine for anesthesia	42	Machine, gas anesthesia/ analgesia, complete systems. Section 868. 5160(b) Gas machine for analgesia is exempt from critical device requirements.
5.	868.5240	Anesthesia breathing circuit.	19	Circuit, breathing (w/ connector, adaptor y-piece).
6.	868.5400	Electroanesthesia apparatus.	6,62	Apparatus, electroanesthesia; and stimulator, electroanesthesia.
7.	868.5440	Portable oxygen generator.	32	Generator, oxygen, portable. #See Pg 25
8.	868.5470	Hyperbaric chamber. (Monoplace)	--	---
9.	868.5610	Membrane lung for long-term pulmonary support.	41	Lung, membrane (for long-term pulmonary support).
10.	868.5650	Esophageal obturator.	2	Airway, esophageal (obturator).
11.	868.5720	Bronchial tube.	66	Tube, bronchial (w/wo connector).
12.	868.5730	Tracheal tube.	67	Tube, tracheal (w/wo connector).
13.	868.5740	Tracheal/bronchial differential ventilation tube.	68	Tube, tracheal/bronchial, differential/ventilation (w/wo connector).

14.	868.5750	Inflatable tracheal tube cuff.	27	Cuff, tracheal tube, inflatable.
15.	868.5800	Tracheostomy tube and tube cuff.	69	Tube, tracheostomy (w/wo connector).
16.	868.5810	Airway connector.	25	Connector, airway (extension).
17.	868.5830	Autotransfusion apparatus.	9	Autotransfusion apparatus.
18.	868.5895	Continuous ventilator.	73,56	Ventilator, continuous (respirator) and respirator, neonatal ventilator
19.	868.5905	Noncontinuous ventilator (IPPB).	75	Ventilator, noncontinuous (respirator).
20.	868.5915	Manual emergency ventilator.	58,70	Manual emergency ventilator; and resuscitator, pulmonary, manual.
21.	868.5925	Powered emergency ventilator.	70	Unit emergency oxygen and resuscitation.
22.	868.5935	External negative pressure ventilator.	74	Ventilator, external body negative pressure, adult (cuirass).

PART 870 - CARDIOVASCULAR DEVICES

23.	870.1025	Arrhythmia detector and alarm.	29	Detector and alarm, arrhythmia.
24.	870.1330	Catheter guide wire.	--	For use with percutaneous transluminal coronary angioplasty catheters. (See #56.)
25.	870.1360	Trace microsphere.	--	---
26.	870.1750	External programmable pacemaker pulse generator.	34	Generator, pulse, pace-maker, external, programmable.
27.	870.1800	Withdrawal-infusion pump.	54	Pump, withdrawal/ infusion.
28.	870.3250	Vascular clip.	22	Clip, vascular.
29.	870.3260	Vena cava clip.	23	Clip, vena cava.
30.	870.3300	Arterial embolization device.	--	---

31.	870.3375	Cardiovascular intravascular filter.	31	Filter, intravascular, cardiovascular
32.	870.3450	Vascular graft prosthesis of less than 6-millimeters diameter.	47,52	Prosthesis, arterial graft synthetic, and prosthesis vascular graft.
33.	870.3460	Vascular graft prosthesis of 6 milli-meters and greater diameter.	47,52	Prosthesis, arterial graft synthetic, and prosthesis, vascular graft.
34.	870.3470	Intracardiac patch or pledget made of poly-propylene. polyethylene polyethylene tere-phthalate, or polytetra-fluoroethylene.	--	---
35.	870.3535	Intra-aortic balloon and control system.	10	Balloon, intra-aortic, and control system.
36.	870.3545	Ventricular bypass (assist) device.	15	Bypass, ventricular (assist).
37.	870.3600	External pacemaker Pulse generator.	33	Generator, pulse, pacemaker, external.
38.	870.3610	Implantable pacemaker pulse generator.	35	Generator, pulse, pace-maker, implantable.
39.	870.3620	Pacemaker lead adaptor.	--	---
40.	870.3650	Pacemaker polymeric mesh bag.	--	---
41.	870.3670	Pacemaker charger.	--	---
42.	870.3680	Cardiovascular permanent or temporary pacemaker, electrode.	30	Electrode, pacemaker, permanent and temporary
43.	87O.3700	Pacemaker programmers.	--	---
44.	870.3710	Pacemaker repair or replacement material.	--	---
45.	870.3800	Annuloplasty ring.	--	---
46.	870.3850	Carotid sinus nerve	--	---

		stimulator.		
47.	870.3925	Replacement heart valve.	71	Valve, heart replacement.
48.	870.4320	Cardiopulmonary bypass pulsatile flow generator.	--	---
49.	870.4350	Cardiopulmonary bypass oxygenator.	44	Oxygenator, cardiopulmonary.
50.	870.4360	Nonroller-type cardiopulmonary bypass blood pump.	13	Blood pump, cardiopulmonary bypass, non-roller.
51.	870.4370	Roller-type cardiopulmonary bypass blood pump.	14	Blood pump, cardiopulmonary bypass roller type.
52.	870.5200	External cardiac compressor.	24,57	Compressor, external, cardiac powered, and resuscitator, cardiac mechanical.
53.	870.5225	External counter-pulsating device.	26	Counter-pulsating device, external.
54.	870.5300	DC-defibrillator (including paddles).	28	Defibrillator, DC-powered (including paddles).
55.	870.5550	External transcutaneous cardiac pacemaker (noninvasive).	45	Pacemaker, cardiac, external transcutaneous.
56.	---	Percutaneous transluminal coronary angioplasty (PTCA) balloon dilation catheter.	--	Premarket approval device.
57.	---	Automatic Implanted Cardioverter Defibril-lator System.	--	Premarket approval device.

PART 872 -- DENTAL DEVICES

58.	872.3640	Endosseous implant.	--	---

PART 874 -- EAR, NOSE, AND THROAT DEVICES

59.	874.3620		Ear, nose and throat synthetic polymer material.	--	---
60.	874.3695		Mandibular implant facial prosthesis.	--	---
61.	874.3730		Laryngeal prosthesis (Taub design).	49	Prosthesis, Laryngeal
62.	874.3820		Endolymphatic shunt	--	---
63.	874.3850		Endolymphatic shunt tube with valve.	--	---
64.	874.3930		Tympanostomy tube with semipermeable membrane	--	---
65.	---		Ear, nose, throat natural polymer - collagen material.	--	Pre-Amendments Device; not classified.

PART 876 -- GASTROENTEROLOGY-UROLOGY DEVICES

66.	876.3350		Penile inflatable implant.	--	---
66a	876.3630		Penile rigidity implant	--	---
67.	876.5270		Implanted electrical urinary continence device.	--	---
68.	876.5540		A-V shunt cannula.	--	Included in blood access device and accessories.
69.	876.5630	#	Peritoneal dialysis system and accessories.	46	Peritoneal dialysis system, automatic delivery
70.	876.5820	#	Hemodialysis system and and accessories. Dialysate concentrate Hollow fiber capillary dialyzers Disposable dialyzers High permeability dialyzers Parallel flow dialyzers Single needle dialysis set Dialysate delivery system	36	Dialysate concentrate added.

 # See charts showing the critical/noncritical breakdown of peritoneal and hemodialysis systems on pages 21 and 22 of Attachment B.

70A	876.5860 #	High permeability hemodialysis system.	36	Dialysate concentrate added.
71.	876.5870	Sorbent hemoperfusion system.	7	Apparatus, hemoperfusion, sorbent.
72.	876.5880	Isolated kidney perfusion and transport system and accessories.	--	---
73.	876.5955	Peritoneo-venous shunt.	--	---
74.	46 FR 7566 (1/23-/81)	Urethral sphincter prosthesis.	51	Prosthesis, urethra sphincter; device-not known to be in commercial distribution.
75.	46 FR 7566 (1/23/81)	Urethral replacement	55	Replacement, urethral. Device not known to be in commercial distribution.

PART 878 -- GENERAL AND PLASTIC SURGERY DEVICES

(The following are class III devices. See 21 U.S.C. 360j(l).)

76.	42 FR 63474 (12/16/77)	Absorbable surgical sutures.	--	Class III transitional device.
77.	42 FR 63474 (12/16/77)	Nonabsorbable surgical sutures.	--	Class III transitional device.
78.	879.4520	Polytetrafluoroethylene (Teflon) injectable.	--	Class III transitional device.
79.	878.3300	Surgical mesh.	--	---
80.	878.3500	Polytetrafluoroethylene with carbon fibers composite implant material.	--	---
81.	878.3530	Inflatable breast prosthesis	--	---
82.	878.3540	Silicone gel-filled breast prosthesis.	--	---
83.	---	Implanted mammary prosthesis of composite saline and gel-filled design.	510(k) device.	
84.	878.3610	Esophageal prosthesis.	48	Prosthesis, esophagus.
85.	878.3720	Tracheal prosthesis.	50	Prosthesis, trachea.
86.	878.4300	Implantable clip.	--	---
87.	878.4750	Implantable staple.	--	---
88.	---	Maxillofacial prosthesis.	--	ENT facial prosthesis, maxillofacial.

PART 880 - GENERAL HOSPITAL AND PERSONAL USE DEVICES

89.	880.5130	Infant radiant warmer.	12	Bed, radiant heat.
90.	880.5400	Neonatal incubator.	37	Incubator, neonatal ventilator.
91.	880.5410	Neonatal transport incubator.	--	---

92.	880.5725	Infusion pump.	53	Term "cardiovascular" dropped since not used in classification regulation and devices not marketed as "cardiovascular infusion pumps."
93.	--	Implanted infusion pump.	--	Premarket approval device.

PART 882 - NEUROLOGICAL DEVICES

94.	882.5030	Methyl methacrylate for aneurysmorrhaphy.	--	---
95.	882.5150	Intravascular occluding catheter.	17	Catheter, intravascular occluding.
96.	882.5200	Aneurysm clip.	20	Clip, aneurysm.
97.	882.5225	Implanted malleable clip.	--	---
98.	882.5250	Burr hole cover.	--	---
99.	882.5300	Methyl methacrylate for cranioplasty	--	---
100.	882.5320	Preformed alterable cranioplasty plate.	--	---
101.	882.5330	Preformed nonalterable cranioplasty plate.	--	---
102.	882.5360	Cranioplasty plate fastener.	--	---
103.	882.5550	Central nervous system fluid shunt and components.	59	Shunt, central nervous system fluid and components.
104.	882.5820	Implanted cerebellar stimulator.	60	Stimulator, cerebella, implanted.
105.	882.5830	Implanted diaphragmatic/ phrenic nerve stimulator.	61	Stimulator, diaphragmatic/ phrenic nerve, implanted.
106.	882.5840	Implanted intracerebral/ subcortical stimulator for pain relief.	63	Stimulator, intracerebral/ subcortical, implanted (pain relief).
107.	882.5850	Implanted spinal cord stimulator for bladder evacuation.	--	---
108.	882.5860	Implanted neuromuscular	--	---

		stimulator.		
109.	882.5870	Implanted peripheral nerve stimulator for pain relief.	--	---
110.	882.5880	Implanted spinal cord stimulator for pain relief.	--	---
111.	882.5880	Epidural spinal electrode.	--	Component of Implanted spinal cord stimulator for pain relief (#110).
112.	882.5900	Preformed craniosynostosis strip.	--	---
113.	882.5910	Dura substitute.	--	---
114.	882.5950	Artificial embolization device.	65	Thromboemboli, intravascular (artificial embolization device).
115.	---	Lyophilized human (cadaver) dura mater.	--	Pre-Amendments device; not classified.
116.	---	Stabilized epidural spinal electrode.	--	Premarket approval device.
117.	---	Implanted intracranial pressure monitor.	--	Premarket approval device.
118.	---	Totally implanted spinal cord stimulator for pain relief.	--	Premarket approval device.

PART 884 - OBSTETRICAL AND GYNECOLOGICAL DEVICES

119.	884.5360	Contraceptive intrauterine device (IUD) and introducer.	38	Intrauterine contraceptive device (IUD) and introducer
120.	884.5380	Contraceptive tubal occlusion device (TOD) and introducer.	11 21 72	Band, tubal occlusion; Clip, tubal Occlusion; Valve, tubal occlusion.

PART 886 - OPHTHALMIC DEVICES

121.	886.3300	Absorbable implant (scleral buckling method)	--	---
122.	886.3400	Keratoprosthesis	39	Keratoprosthesis, non-custom
123.	886.3600	Intraocular lens	40	Lens, intraocular, ophthalmic; Class III transitional device.
124.	886.3920	Eye valve implant	--	---

PART 888 ORTHOPEDIC DEVICES

125.	888.3000	Bone Cap.	--	---
126.	888.3010	Bone fixation cerclage.	--	---
127.	888.3020	Intramedullary fixation rod.	--	---
128.	888.3025	Passive tendon prosthesis.	--	---
129.	888.3027	Polymethylmethacrylate (PMMA) bone cement.	--	Class III transitional device.
130.	888.3030	Single/multiple component metallic bone fixation appliances and accessories.	--	---
131.	888.3040	Smooth or threaded metallic bone fixation fastener.	--	---
132.	888.3050	Spinal interlaminal fixation orthosis.	--	---
133.	888.3060	Spinal intervertebral body fixation orthosis	--	---

134.	888.3100	Ankle joint metal/composite semi-constrained cemented prosthesis.	--	---
135.	888.3110	Ankle joint metal/polymer semi-constrained cemented prosthesis.	--	---
136.	888.3120	Ankle joint metal/polymer non-constrained cemented prosthesis.	--	---
137.	888.3150	Elbow joint metal/metal or metal/polymer constrained cemented prosthesis.	--	---
138.	888.3160	Elbow joint metal/polymer semi-constrained cemented prosthesis.	--	---
139.	888.3170	Elbow joint radial (hemi-elbow) polymer prosthesis.	--	---
140.	888.3180	Elbow joint humeral (hemi-elbow) metallic uncemented prosthesis.	--	---
141.	888.3200	Finger joint metal/metal constrained uncemented prosthesis.	--	---
142.	888.3210	Finger joint metal/metal constrained cemented prosthesis.	--	---
143.	888.3220	Finger joint metal/polymer constrained cemented prosthesis.	--	---
144.	888.3230	Finger joint polymer con-strained prosthesis.	--	---
145.	888.3300	Hip joint metal constrained cemented or uncemented prosthesis.	--	---
146.	888.3310	Hip joint metal/polymer constrained cemented or uncemented prosthesis.	--	---

147.	888.3320	Hip joint metal/metal semi-constrained, with a cemented acetabular component, prosthesis.	--	---
148.	888.3330	Hip joint metal/metal semi-constrained, with an uncemented acetabular component, prosthesis.	--	---
149.	888.3340	Hip joint metal/composite semi-constrained cemented prosthesis.	--	---
150.	888.3350	Hip joint metal/polymer semi-constrained cemented prosthesis.	--	---
151.	888.3360	Hip Joint femoral (hemi-hip) metallic cemented or uncemented prosthesis.	--	---
152.	888.3370	Hip joint (hemi-hip) acetabular metal cemented prosthesis.	--	---
153.	888.3380	Hip joint femoral (hemi-hip) trunnion-bearing metal/polyacetal cemented prosthesis.	--	---
154.	888.3390	Hip joint femoral (hemi-hip) metal/polymer cemented or uncemented prosthesis.	--	---
155.	888.3400	Hip joint femoral (hemi-hip) metallic resurfacing prosthesis.	--	---
156.	888.3410	Hip joint metal/polymer semi-constrained resur-facing cemented prosthesis.	--	---
157.	888.3480	Knee joint femorotibial metallic constrained cemented prosthesis.	--	---
158.	888.3490	Knee joint femorotibial	--	---

		metal/composite non-constrained cemented prosthesis.		
159.	888.3500	Knee joint femorotibial metal/composite semi-constrained cemented prosthesis.	--	---
160.	888.3510	Knee joint femorotibial metal/polymer con-strained cemented prosthesis.	--	---
161.	888.3520	Knee joint femorotibial metal/polymer non-constrained cemented prosthesis.	--	---
162.	888.3530	Knee joint femorotibial metal/polymer semi-constrained cemented prosthesis.	--	---
163.	888.3540	Knee joint patellofemoral polymer/metal semi-constrained cemented prosthesis.	--	---

164.	888.3550	Knee joint patellofemoro-tibial polymer/metal/ metal constrained cemented prosthesis.	--	---
165.	888.3560	Knee joint patellofemoro-tibial polymer/metal/ polymer semi-constrained cemented prosthesis.	--	---
166.	888.3570	Knee joint femoral (hemi-knee) metallic uncemented prosthesis.	--	---
167.	888.3580	Knee joint patellar (hemi-knee) metallic resur-facing uncemented prosthesis.	--	---
168.	888.3590	Knee joint tibial (hemi-knee) metallic resur-facing uncemented prosthesis.	--	---
169.	888.3640	Shoulder joint metal/metal or metal/polymer constrained cemented prosthesis.	--	---
170.	888.3650	Shoulder joint metal/ polymer non-constrained cemented prosthesis.	--	---
171.	888.3660	Shoulder joint metal/ polymer semi-constrained cemented prosthesis.	--	---
172.	888.3680	Shoulder Joint glenoid-- (hemi- shoulder) metallic cemented prosthesis.	---	
173.	888.3690	Shoulder joint humeral (hemi- shoulder) metallic uncemented prosthesis.	--	---

174.	888.3720	Toe joint polymer constrained prosthesis.	--	---
175.	888.3730	Toe joint phalangeal (hemi-toe) polymer prosthesis.	--	---
176.	888.3750	Wrist joint carpal lunate polymer prosthesis.	--	---
177.	888.3760	Wrist joint carpal scaphoid Polymer prosthesis.	--	---
178.	888.3770	Wrist joint carpal trapezium polymer prosthesis.	--	---
179.	888.3780	Wrist joint polymer constrained prosthesis.	--	---
180.	888.3790	Wrist joint metal constrained cemented prosthesis.	--	---
181.	888.3800	Wrist joint metal/polymer semi-constrained cemented prosthesis.	--	---
182.	888.3810	Wrist joint ulnar (hemi-wrist) polymer prosthesis.	--	---

PERITONEAL DIALYSIS SYSTEMS AND ACCESSORIES

INDIVIDUAL DEVICE	COMPONENT	ACCESSORY	CRITICAL	
			YES	NO
Semi-auto Peritoneal Dialysis System			X	
Auto. Peritoneal Dialysis System			X	
Single-Use Peritoneal Catheter			X	
Long-Term Peritoneal Catheter			X	
		Stylet		X
		Trocar		X
		Obturator		X
		Disposable Administration Set	X	
		Peritoneal Dialysate Fileter		X

As of this time, the following peritoneal dialysate products are considered drugs and are registered by the CDER: sterile prepackaged dialysate and dialysate solutions for peritoneal dialysis.

HEMODIALYSIS SYSTEMS AND ACCESSORIES

INDIVIDUAL DEVICE	COMPONENT	ACCESSORY	CRITICAL	
			YES	NO
Conventional Dialyzer			X	
Dialysate Delivery			X	
	Water Purification System		X	
	Monitor & Control Mechanisms		X	
	Alarms		X	
		Unpowered HD Chair w/o Scale		X
		Powered HD Chair w/o Scale		X
		Dialyzer Holder Set		X
		Dialysis Tie Gun & Ties		X
		Hemodialysis Start/Stop Tray		X
		Hemodialysis Concentrate	X	
Extracorporeal Blood System			X	
	Tubing		X	
	Pumps		X	
	Pressure Monitors		X	
	Air Foam or Bubble Detectors		X	
	Alarms		X	

* Water purification systems when part of the dialysis delivery system.

ATTACHMENT B-1

"SIGNIFICANT RISK DEVICES" *

ANESTHESIOLOGY

Gas machines for analgesia.

CARDIOVASCULAR

Artificial heart, permanent implant and short term use.
Coronary artery retroperfusion system.
Laser coronary angioplasty device.
Percutaneous conduction tissue ablation electrode.

DENTAL

Total temporomandibular joint (TMJ) prosthesis.
TMJ implants.
Glenoid fossa prosthesis.
Mandibular condyle prosthesis.
Interarticular disc prosthesis.
Collagen for any dental use.
Bone filling and augmentation materials.
Absorbable materials.
Subperiosteal implants.

EAR, NOSE AND THROAT

Total ossicular prosthesis replacement.

GASTROENTEROLOGY AND UROLOGY

Endoscope and/or accessories.
Extracorporeal hyperthermia system.
Extracorporeal photophersis system.
Extracorporeal shock-wave lithotriptor.
Mechanical/hydraulic incontinence devices.

* Defined according to 21 CFR 812.3 (m), Definitions for Investigational Device Exemptions. Significant risk devices that are also critical devices are included in the preceding advisory list of devices that are intended for surgical implant or sustaining life in Attachment B.

GENERAL MEDICAL USE

Catheters: Cardiology - diagnostic and treatment types.
Gastroenterology and urology - biliary and urologic.
General hospital - long-term percutaneous, implanted, subcutaneous and intravascular.

Collagen implant material for use in orthopedics and plastic surgery.
Lasers for use in Ob/Gyn, cardiology, gastroenterology, urology, pulmonary, ophthalmology and neurology. Tissue adhesives for use in neurology, gastroenterology, ophthalmology, general and plastic surgery, and cardiology.

GENERAL AND PLASTIC SURGERY

Absorbable hemostatic agents.
Artificial skin.
Injectable silicone.
Silicon gel filled angelchik reflux valve.
Silicon gel filled chin prosthesis.

OBSTETRICS AND GYNECOLOGY

Cervical dilator.
Chorionic villus sampling catheter, phase II (pregnancy continued to term).
Contraceptive devices: cervical cap, diaphragm, and sponge.
Silicone gel filled testicular prosthesis.

OPHTHALMICS

Extended wear contact lens.
Retinal reattachment systems: sulfur hexafluoride, silicone oil, tacks, perfluropropane.

ORTHOPEDICS

Implantable ligament prostheses.
Bone growth stimulator.
Calcium tri-phosphate/hydroxyapatite ceramics.
Xenografts

RADIOLOGY

Hyperthermia systems and applicators.

SUPPLEMENTAL INFORMATION

* With regard to portable oxygen generators, the molecular sieve, or oxygen concentrator device, is not considered a critical device for purposes of applying the QS/GMP, when it is intended for home respiratory therapy use.*

ATTACHMENT C

MODEL WARNING LETTER
(QS/GMPs and MDR)

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

RESPONSIBLE INDIVIDUAL, TITLE
ESTABLISHMENT NAME
ESTABLISHMENT'S COMPLETE ADDRESS

Dear (Addressee):

During an inspection of your establishment located in (city, state), on (dates), our investigator(s) determined that your establishment manufactures (generic type of device). (Generic name of device) are devices as defined by Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The above-stated inspection revealed that these devices are adulterated within the meaning of Section 501(h) of the Act, in that the methods used in, or the facilities or controls used for manufacturing, packing, storage, or installation are not in conformance with the Quality System regulation for medical devices, as specified in Title 21, Code of Federal Regulations (CFR), Part 820, as follows:

1. Failure to conduct planned and periodic audits of the quality assurance program in accordance with written procedures. For example, no audits of the quality assurance program have been performed for at least 3 years.

2. Failure to investigate the failure of a device to meet performance specifications after a device has been released for distribution, and to make a written record of the investigation including conclusions and follow-up. For example, there are no records of failure investigations for Model ____, S/N ____, and Model __, S/N ____, which were returned because they did not operate properly.

3. Failure to maintain device history records for Model ___ to demonstrate that the devices are manufactured in accordance with the device master record.

4. Failure to immediately review, evaluate and investigate any complaint pertaining to injury, death, or any hazard to safety. For example, there is no record of the investigation of a report that a child's death associated with the use of Model ___ at the Community Medical Center on/or about February 8, 1997.

Additionally, the above stated inspection revealed that your devices are misbranded within the meaning of Section 502(t)(2) of the Act, in that your establishment failed to submit information to the Food and Drug Administration as required by the Medical Device Reporting (MDR) Regulation, as specified in 21 CFR Part 803. Specifically, you failed to submit an MDR report to FDA after receiving information which reasonably suggested that one of your commercially distributed devices may have caused or contributed to a death. The February 8, 1997, incident report from the Community Medical Center in which a child standing in a crib fell over, caught his head in a "Y" formed by the crib rail and end post, and died, should have been reported as a death.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the Form FDA-483 issued at the conclusion of the inspection may be symptomatic of serious underlying problems in your establishment's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Additionally, no premarket submissions for Class III devices to which the Quality System/GMP deficiencies are reasonably related will be cleared or approved until the violations have been corrected. Also, no requests for Certificates to Foreign Governments will be approved until the violations related to the subject devices have been corrected.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil penalties.

Please notify this office in writing within 15 working days of receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to identify and make corrections to any underlying systems problems necessary to assure that similar violations will not recur. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

Your response should be sent to (name), Compliance Officer, Food and Drug Administration, (street address), (city, state & zip code).

Sincerely yours,

District Director
_____ District

ATTACHMENT C

FOR USE WHEN FOLLOWING THE ENFORCEMENT STRATEGY FOR ESTABLISHMENTS WITH REPEATED VIOLATIVE INSPECTIONS (Part V, A.5.c.).

MODEL WARNING LETTER
(QS/GMP's and MDR)

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

RESPONSIBLE INDIVIDUAL, TITLE
ESTABLISHMENT NAME
ESTABLISHMENT'S COMPLETE ADDRESS

Dear (Addressee):

During an inspection of your establishment located in (city, state), on (dates), our investigator(s) determined that your establishment manufactures (generic type of device). (Generic name of device) are devices as defined by Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The above-stated inspection revealed that these devices are adulterated within the meaning of Section 501(h) of the Act, in that the methods used in, or the facilities or controls used for manufacturing, packing, storage, or installation are not in conformance with the Quality System/Good Manufacturing Practice (QS/GMP) for Medical Devices Regulation, as specified in Title 21, Code of Federal Regulations (CFR), Part 820, as follows:

1. Failure to conduct planned and periodic audits of the quality assurance program in accordance with written procedures. For example, no audits of the quality assurance program have been performed for at least 3 years.

2. Failure to investigate the failure of a device to meet performance specifications after a device has been released for distribution, and to make a written record of the investigation including conclusions and follow-up. For example, there are no records of failure investigations for Model ____, S/N ____, and Model __, S/N ____, which were returned because they did not operate properly.

3. Failure to maintain device history records for Model ___ to demonstrate that the devices are manufactured in accordance with the device master record.

4. Failure to immediately review, evaluate and investigate any complaint pertaining to injury, death, or any hazard to safety. For example, there is no record of the investigation of a report that a child's death associated with the use of Model ___ at the Community Medical Center on/or about February 8, 1997.

Additionally, the above stated inspection revealed that your devices are misbranded within the meaning of Section 502(t)(2) of the Act, in that your establishment failed to submit information to the Food and Drug Administration as required by the Medical Device Reporting (MDR) Regulation, as specified in 21 CFR Part 803. Specifically, you failed to submit an MDR report to FDA after receiving information which reasonably suggested that one of your commercially distributed devices may have caused or contributed to a death. The February 8, 1997, incident report from the Community Medical Center in which a child standing in a crib fell over, caught his head in a "Y" formed by the crib rail and end post, and died, should have been reported as a death.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the Form FDA-483 issued at the conclusion of the inspection may be symptomatic of serious underlying problems in your establishment's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Additionally, no premarket submissions for Class III devices to which the QS/GMP deficiencies are reasonably related will be cleared until the violations have been corrected. Also, no requests for Certificates to Foreign Governments will be approved until the violations related to the subject devices have been corrected.

In order to facilitate FDA in making the determination that such corrections have been made and thereby enabling FDA to withdraw its advisory to other federal agencies concerning the award of government contracts, and to resume marketing clearance for Class III devices for which a 510(k) premarket notification or Premarket Approval application (PMA) has been submitted, and Certificates to Foreign Governments for products manufactured at [x] facility, we are requesting that you submit to this office on the schedule below[1], certification by an outside expert consultant that he/she has conducted an audit of your establishment's manufacturing and quality assurance systems relative to the requirements of the device QS/GMP regulation (21CFR, Part 820). You should also submit a copy of the consultant's report, and certification by your establishment's Chief Executive Officer (if other than yourself) that he or she has reviewed the consultant's report and that your establishment has initiated or completed all corrections called for in the report. The attached guidance may be helpful in selecting an appropriate consultant.

The initial certifications of audit and corrections and subsequent certifications of updated audits and corrections (if required) should be submitted to this office by the following dates:

- Initial certifications by consultant and establishment -Show actual date (allow approximately six months from issuance of Warning Letter).

[1] This policy is intended to address a situation where a manufacturer has failed to maintain an adequate quality assurance system over a period of several years. Requesting certifications of compliance subsequent to the initial certification is intended to help a manufacturer institutionalize an adequate quality assurance system. Districts have the option, however, of not asking for subsequent reports or varying the period over which subsequent reports may be requested.

- Subsequent certifications-Show actual date(s). You may ask for annual reports for two years after the follow-up inspection.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil penalties.

Please notify this office within 15 days of receipt of this letter, of the specific steps you will be taking to comply with our request.

Your response should be sent to (name), Compliance Officer, Food and Drug Administration, (street address), (city, state & zip code).

Sincerely yours,

District Director

_____ District

The following guidance was originally published in the CDRH, Office of Compliance Industry Letter No. 2, dated July 6, 1993.

SELECTING A CONSULTANT ?

As the number of consultants has increased in the past few years, so too has our concern about their qualifications and the quality of their work. While most consultants accurately and honestly promote their capabilities, we believe the device industry should exercise diligence in the selection of a consultant. It is very disappointing to see a company which is experiencing serious problems go to the expense of hiring a consultant who fails to constructively contribute to the restoration of the company's regulatory health.

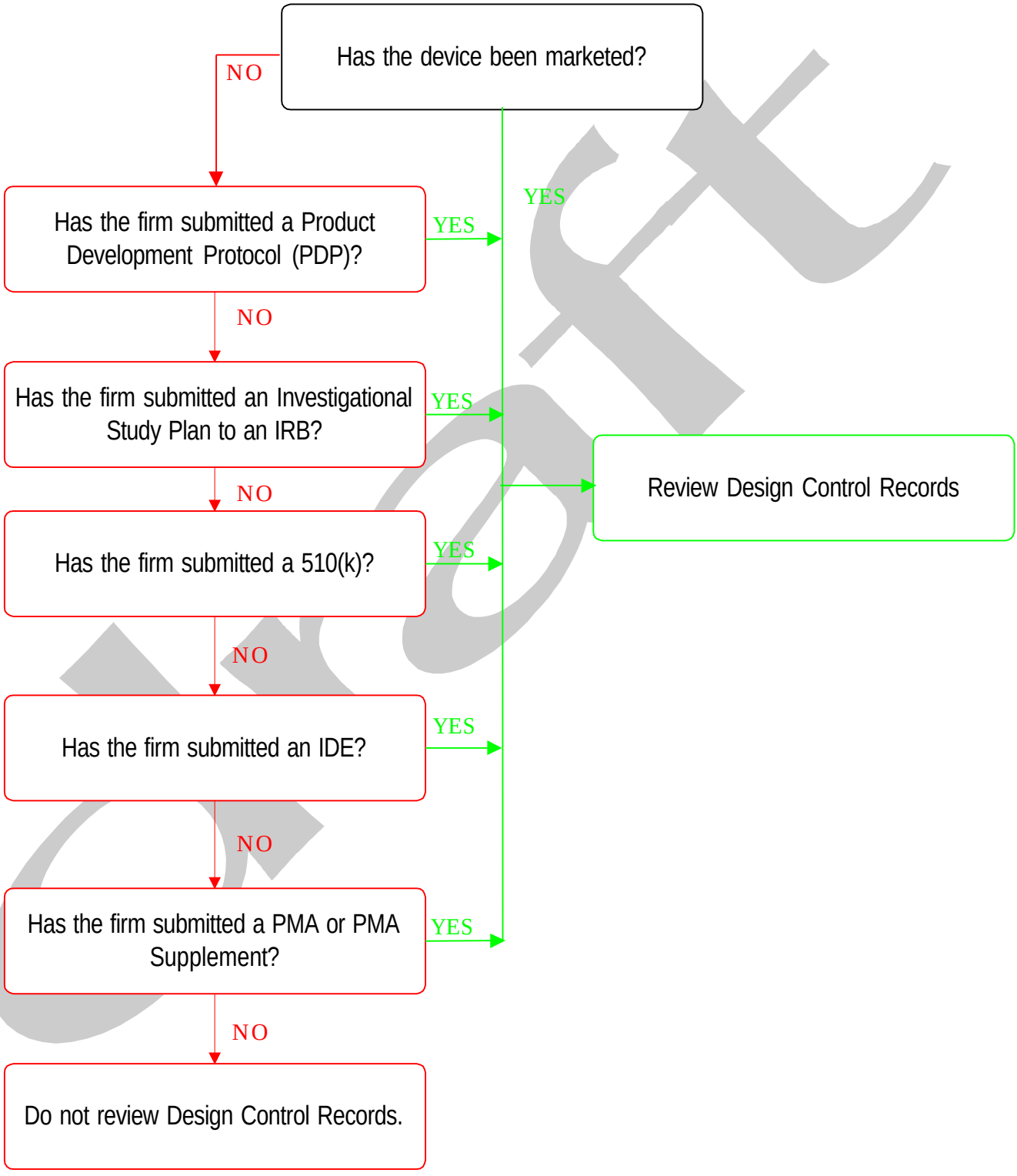
Of course, FDA cannot recommend or endorse a particular consultant, but we can offer some criteria that should be considered when selecting one. You should first determine what type of consultant you need. There are basically three types of consultants: regulatory, quality, and technical. A regulatory consultant is one that will specialize in 510(k) and PMA issues, QS/GMP's and/or device labeling. A quality consultant is adept at QS/GMP auditing, and writing and revising procedures. The technical consultant basically knows how to find problems and fix them. In some cases a company may need the services of one or more of these consultants. The ideal consultant would be highly qualified in all three of these areas. Since we in compliance deal most with QS/GMP issues, we have identified some factors that we recommend you consider when selecting a quality consultant, but these factors may have applicability for the other types of consultants also:

- How long has the consultant worked with the device (not drug) QS/GMP regulation?
- Is his/her knowledge current?
- Does he/she know what CDRH's "current" policies and interpretations are for device QS/GMP's?
- Does the consultant sponsor/participate in training courses?
- Is he/she frequently asked to give presentations at FDA/industry sponsored seminars? What have been the reactions to these presentations?
- One of the primary attributes of a good consultant is to be a "good communicator". He/she must be able to communicate problems and provide solutions in a clear, concise manner, and in such a way that the company knows how to perform corrections the "right" way, the first time.
- Has he/she been deposed and/or testified as an expert witness, either for the FDA or for industry?
- Obtain a listing of the consultant's clients over the last several years. Check these references!
- What types of certifications does the consultant have, i.e., Is the certification recognized by professional societies, etc?

We believe that a little homework in identifying and selecting a consultant will have long term payoffs for any company.

Decision Chart A

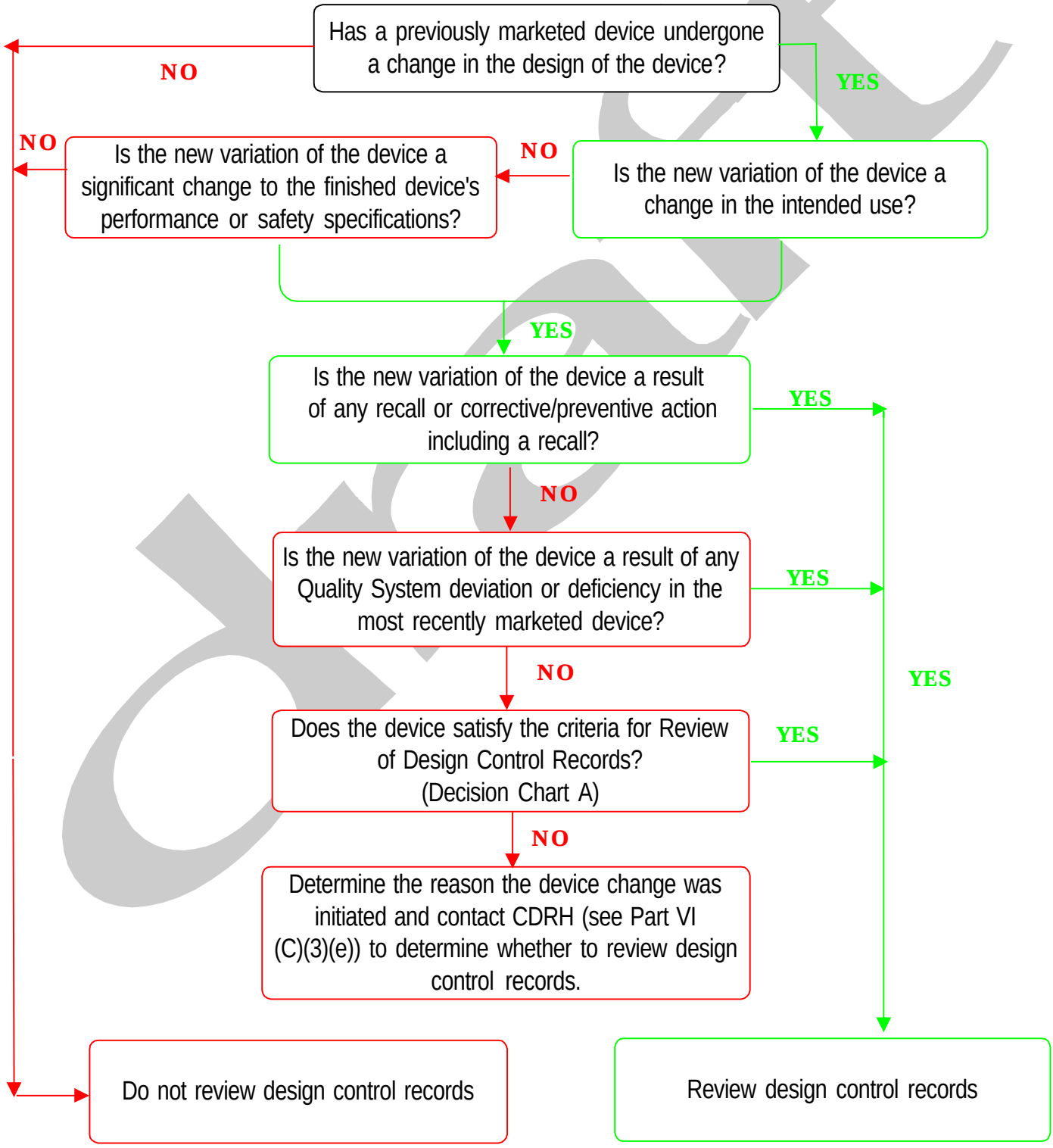
Review of Design Control Records *



* Investigators may review design control records at any stage in the design and development process when a manufacturer consents to their review.

Decision Chart B

Review of Design Control Records for Device "Changes"



ATTACHMENT E

SUMMARY OF MDR REPORTING REQUIREMENTS

Individual Adverse Event Reports - 803.50

[ ] General Requirements:

- Manufacturers must submit death, serious injury, and malfunction reports within 30 days after they become aware of a reportable event.

- The information can come from any source.

- Devices that "may have caused or contributed" to a death or serious injury; or a malfunction that would be likely to cause or contribute to a death or serious injury must be reported.

[ ] Reasonably known:

- Firms must provide all information that is reasonably known to them. FDA considers the following to meet this standard, i.e., any information:

- that can be obtained by contacting a user facility, distributor, and/or other initial reporter,

- in the manufacturer's possession,

- that can be obtained by analysis, testing, or other evaluation of the device.

[ ] Information required to be reported:

- The form FDA 3500A is the primary reporting form for death, serious injury and malfunction events. With the exception of drug or biologic related items, all the fields must be completed or have an entry (NA, NI, OR UNK) indicating why the information could not be obtained.

[ ] Missing Information:

- Manufacturers are responsible for obtaining and providing FDA with any information that is missing from reports that are received from user facilities, distributors, and other initial reporters.

- If a firm cannot provide complete information, it must provide a statement explaining why such information was incomplete and the steps taken to obtain the information.

- Any required information not available at the time of the report, obtained at a later date, must be forwarded to FDA in a supplemental report within 1 month of receipt.

[ ] Investigation:
- Manufacturers are responsible for investigating and evaluating the cause of each event.

- These investigations must follow the requirements in 820.198 and provide the information required on form FDA 3500A, Block H.6, H.7, and H.9.

[ ] Five-Day Reports - 803.53:
- Manufacturers must submit a five-day report on form FDA 3500A within five days under the following two conditions:

a. They become aware that an MDR reportable event, from any source, requires remedial action to prevent an unreasonable risk of substantial harm to the public health.

OR

b. They receive an FDA written request for the submission of five-day reports.

[ ] Baseline Reports - 803.55:
- Manufacturers are required to submit a baseline report on FDA 3417 form when the device model is first reported under 803.50.

- Baseline Reports must be updated annually (if information changes) on the firm's scheduled registration date, per Part 807.21.

NOTE: The following MDR requirements have been stayed or revoked

1. Certification, 21 CFR 803.57,
2. U.S. Designated Agent requirements, 21 CFR 803.58, 807.3, 807.20 and 807.40, and
3. Baseline Reports, only sections 21 CFR 803.55(b) (9) and (10), which correlate to items 15 and 16 on the Baseline Report form, FDA 3417.

[ ] Supplemental Reports - 803.56:
- Manufacturers are required to submit, within one month after receipt, any required information that was not available to them during the initial 30 day reporting requirement for deaths, serious injuries, malfunctions. This also includes five-day reports.

GENERAL MDR GUIDANCE

This document provides general guidance regarding the reporting of adverse events required by the Medical Device Reporting (MDR) Regulation.

A. PER SE RULE

This requirement no longer exists. Therefore, the submission of an event by a health care professional does not require the manufacturer to report the event based solely on the statements of a health care professional. The event must meet the reporting criteria in MDR to qualify as a reportable event.

B. REPORTING TIME FRAMES

Firms now have up to 30 CALENDAR days after they become aware of a device related death, serious injury or malfunction before they are required to submit a report to FDA.

C. FIVE-DAY REPORTS

If a firm has initiated a **remedial** action, as a result of an MDR reportable event, and the action is being taken to prevent an **unreasonable** risk of substantial harm to the public health, a report is required within five work days of becoming aware. NOTE: Five day reports are not required for all **remedial** action, the action must be taken to prevent an **unreasonable** risk of substantial harm to he public health.

D. NON-REPORTABLE EVENTS

Firms must submit MDR reports when the reported information reasonably suggests an association between one of its devices and a reportable death, serious injury or malfunction. Under some circumstances, an adverse event may appear to trigger the requirement of submission of an MDR, but because information reveals the device did not cause or contribute to the death or serious injury, no MDR is required.

Basically, a firm is required to submit an MDR report when it becomes aware of information reasonably suggesting that an event meets the criteria for reporting a Death, Serious Injury, or Malfunction. For example, a hospital informs a manufacturer that its device has failed and, as a result, a patient died. At this point, the firm has become aware of information that reasonably suggests they are in receipt of a reportable MDR event.

Next, the firm must investigate the report to determine its cause. Both the QSR & MDR require investigation of complaints. During its investigation a firm may become aware of information that changes the initial report's conclusions. For example, the firm may find that its device was not involved in the death and could not have caused or contributed to the death. In these instances the firm would document the information that changes the association between its device and the death. No report would be required if the death or other facts turn out to be incorrect. But, if the firm becomes aware of the identity of the device/firm that was associated with the death, the firm is responsible for forwarding the information to the FDA.

However, if the firm's investigation does not change the alleged association between the device and the death, the event must be submitted as an MDR report. In addition, if the firm's investigation obtains information that would cause a person who is qualified to make a medical judgment reach a reasonable conclusion that the device did not cause or contribute to a reportable MDR event - no report is required. Translation - if a firm decides NOT to report an apparent device-related Death, Serious Injury or Malfunction - this decision must be made by a person that the regulation recognizes as qualified to make a medical judgment, i.e., a physician, nurse, risk manager, or biomedical engineer. Using the example from above, if the firm's investigation yields an autopsy finding that the patient died from cancer – not the device - the firm could decide NOT to report as long as the decision is consistent with the regulation:

1. There is documented information that changes the association between the death and the device,

2. The decision is made by a person who is qualified to make a medical Judgement, and

3. The conclusion reached by the person in item two is reasonable.

PLEASE NOTE THE FOLLOWING:

- Firms ARE NOT required to have every MDR report reviewed by a person qualified to make a medical judgement and/or a person with a medical degree or training. Individuals who are not qualified to make a medical judgement can review MDR reports and make decisions on the basis of facts but they cannot make decisions NOT to report MDR events that require medical judgement.

- In lieu of in-house or on - site qualified medical personnel or individuals qualified to make a medical judgement the firm may use consultants.

- When reviewing a non-reportable events validate/document the credentials of the individual making these decisions as well as the decision/documents for not reporting the event.

E. INVESTIGATION

Firms are required to investigate EVERY device related death, serious injury and malfunction in accordance with QS/GMP regulation, 820.198. Failure to comply with this provision is a violation of BOTH the QS/GMP regulation and MDR. Manufacturers are also required to VERIFY information on each form FDA 3500A as well as make a good faith effort to obtain information that is missing/not provided by the reporter. If the firm cannot obtain the missing information, the MDR complaint files shall contain an explanation of why the information could not be obtained as well as documentation of the firm's efforts to obtain the missing information.

F. REASONABLY KNOWN INFORMATION

FDA considers information that can be obtained by contacting the reporter is in the possession of a firm, and can be obtained by analysis, testing, or other evaluation of a device to be information that a firm is expected to REASONABLY know, obtain and report.

G. REASONABLY KNOWN/GOOD FAITH EFFORT

A firm must demonstrate that it exercised "good faith" in any failed attempts to obtain required data that is missing, incorrect, or that FDA considers to be reasonably known. While the concept of good faith is generally considered to be equivalent to "due diligence", CDRH has not developed a standard. However, the firm's procedures for obtaining missing information should appear under the "Internal Systems" section of its written MDR procedures. In addition, the Center believes that the parameters of good faith effort must, at a minimum, comport with the level of risk/nature of the device associated with the event being investigated.

H. SERIOUS INJURY

The interpretation of what constitutes a serious injury can be subjective and complicate the enforcement of MDR. The "unanticipated temporary impairment" part of the former serious injury definition has been rescinded, thus

alleviating a source of subjectivity. In addition, the requirements that intervention be "immediate" and the concept of "probability" have also been removed from the serious injury definition.

The current MDR regulation states that a serious injury is an "injury or illness." This literally means that there has to be a injury that is life-threatening, results in permanent impairment/damage, or necessitates medical/surgical intervention to preclude permanent impairment/damage in order for an event to be reportable as a serious injury. If there is no injury attributable to the device, then there is no serious injury report, however, the event may qualify as an MDR reportable malfunction depending upon the circumstances.

The Center may decide to clarify the definition of serious injury. These categories will be provided to the field and the industry through MDR guidance documents and/or letters, as necessary.

I. MALFUNCTIONS

Malfunction reporting decisions have been the subject of concern by both industry and the FDA. Basically, a malfunction is an event that is likely to cause or contribute to either a death or serious injury, but some circumstance prevented the injury or death from occurring. These events are very important since they represent "potential" deaths or serious injuries and provide the Agency with the opportunity to be proactive in reducing risks. Not all malfunctions, however, are MDR reportable events.

If a malfunction has never led to a death or a serious injury, and a firm can document this conclusion, it is not reportable. This rule applies UNLESS there is a compelling clinical evaluation to indicate that the event would be likely to cause or contribute, even though a previous death/serious injury had not occurred.

If a malfunction is not MDR reportable it may be a complaint and thus subject to the QS/GMP complaint handling requirements. Determining if an event is a reportable malfunction involves a series of challenges:

1. Is the event device-related,

2. Has it failed to perform its intended function/meet its performance specifications, and

3. Is this failure likely to cause or contribute to a death

or serious injury if the event were to happen again.

There is a presumption in MDR that if the event happened once it can happen again. The determination of whether to submit a report should be based on the potential outcome. For example, if this malfunction were to occur, how would it affect the patient? If the answer is "it's likely to cause or contribute to death or serious injury" then the event is reportable. The preamble offers the following guidance, i.e., a malfunction report is required when:

1. The chance of a death or serious injury occurring as a result of the recurrence of the malfunction is not remote;

2. The consequences of the malfunction affect the device in a catastrophic manner that may lead to a death or serious injury;

3. The malfunction results in the failure of the device to perform its intended essential function and compromises the device's therapeutic, monitoring or diagnostic effectiveness, which could cause or contribute to a death or serious injury.

   NOTE: The essential function of a device refers, not only to the device's labeled use, but for any use widely prescribed within the practice of medicine.

4. The malfunction involves a long-term implant or a device that is considered to be life-supporting or life-sustaining and thus is essential to maintaining human life. Malfunctions of long-term implants are not routinely or "automatically" reportable unless the malfunction is likely to cause or contribute to a death or serious injury if it recurs.

5. The manufacturer takes or would be required to take an action under sections 518 or 519(f) of the Act as a result of the malfunction of the device or other similar devices.

   Conversely, malfunctions ARE NOT REPORTABLE if they are not likely to result in a death, serious injury, or another malfunction.

SOURCES OF INFORMATION

WHERE TO OBTAIN MDR FORMS

1. Consolidated Forms and Publications Office
   Washington Commerce Center
   3222 Hubbard Rd.,
   Landover, MD 20785
   NOTE: Form FDA 3500A ONLY

2. Division of Small Manufacturers Assistance
   Office of Health and Industry Programs
   Center for Devices and Radiological Health
   1350 Piccard Drive (HFZ 220)
   Rockville, MD 20850
   NOTE: AVAILABLE ONLY THROUGH FACTS-ON-DEMAND SYSTEM

3. Food and Drug Administration
   MEDWATCH (HF-2)
   5600 Fishers Lane
   Room 9-57
   Rockville, MD 20850
   301-827-7240
   NOTE: FORMS FDA 3500 and 3500A ONLY

4. Web page
   HTTP://www.fda.gov/cdrh/mdr.html

WHERE TO SUBMIT ALL MDR REPORTS

Food and Drug Administration
Center for Devices and Radiological Health
PO Box 3002
Rockville, MD 20857-001

NOTE: Envelopes shall be specifically identified with the type of report enclosed, e.g., User Facility Report, Semiannual Report, Five-Day Report, etc.,

WHERE TO OBTAIN MDR GUIDANCE DOCUMENTS/OTHER MDR INFORMATION

1. CDRH Facts-On-Demand, telephone number 1-800-899-0381 or 301-827-0111. After connecting, follow the recorded instructions. The system allows for one request per call. Enter the shelf number of choice from the list below followed by the # (pound) sign and continue with the programmed prompts.

MDR DOCUMENTS FROM FACTS-ON-DEMAND SYSTEM

SHELF NO.	TITLE
336 #	Final MDR Regulation, published 12/11/95, 77 pages
407#	Baseline Report, Form FDA 3417
799 #	MDR Related Documents Information
853#	Instructions and Coding Manual for Medwatch 3500A
854#	Medwatch FDA Form 3500A
1061#	Instructions for completing form 3417 Baseline report
1096#	Stay of effective date for denominator data on baseline report
1336#	Amendment to final rule, Federal Register, 4/11/96
1074#	Stay of Certification and U.S. Designated Agent requirements, Federal Register, 7/23/96
1075#	Reproposal of Certification requirement, Federal Register, 7/23/96.

2. FDA Internet Home Page (HP)

   a. http://www.fda.gov. - once connected select the CDRH icon.

   b. The CDRH home page can be contacted directly using the address http://www.fda.gov/cdrh/.

ATTACHMENT F

SUMMARY OF TRACKING REQUIREMENTS

WHO IS SUBJECT TO TRACKING ?

- Domestic/Foreign Manufacturers and Importers of tracked devices

WHAT DEVICES ARE SUBJECT TO TRACKING ?

1. Total Temporomandibular joint prosthesis
2. Glenoid fossa prosthesis
3. Mandibulary condyle prosthesis
4. Ventricular bypass (assist) device
5. Implantable pacemaker pulse generator
6. Cardiovascular permanent pacemaker electrode
7. Replacement heart valve
8. Automatic implantable cardioverter/defibrillator
9. Implantable cerebellar stimulator
10. Implanted diaphragmatic/phrenic nerve stimulator
11. Implantable infusion pump
12. Breathing frequency monitor (apnea monitor) including ventilatory efforts monitor
13. Continuous ventilator
14. DC-defibrilator
15. Infusion Pumps - except for those designate and labeled for use exclusively for fluids with low potential risks, e.g., enteral feeding, anti-infective.

WHAT A MANUFACTURER'S TRACKING SYSTEM IS REQUIRED TO DO FOR:

A. - TRACKED DEVICES THAT HAVE NOT BEEN DISTRIBUTED TO A PATIENT
- provide FDA - within 3 working days of a request - the name, address and telephone number of the distributor, multiple distributor, or final distributor holding the device for distribution and the location of the device.

B. - LIFE SUSTAINING DEVICES OR LIFE SUPPORTING DEVICES THAT ARE:
- USED OUTSIDE A DEVICE USER FACILITY,
- INTENDED FOR USE BY A SINGLE PATIENT OVER THE LIFE OF THE DEVICE, AND
- TRACKED PERMANENT IMPLANTS AFTER DISTRIBUTION OR IMPLANTATION IN A PATIENT.

- Upon request provide FDA, within 10 working days:
- the lot number, batch number, model number, or serial number

of the device or other identifier necessary to provide for effective tracking of the device.

- the date the device was shipped by the manufacturer.

- the name, mailing address, and telephone number of the prescribing physician.

- the name, mailing address, and telephone number of the physician regularly following the patient if different than the prescribing physician.

- If applicable, the date the device was explanted and the name, mailing address, and telephone number of explanting physician; the date the patient's death; or the date the device was returned to the manufacturer permanently retired from use, or otherwise permanently disposed of.

C. LIFE SUPPORTING OR LIFE SUSTAINING DEVICES THAT ARE:
- USED OUTSIDE DEVICE USER FACILITIES,
- INTENDED FOR USE BY MORE THAN ONE PATIENT,
- DISTRIBUTED TO THE MULTIPLE DISTRIBUTOR

- Upon request provide FDA within 10 Working Days:
- the lot, model number, batch number, serial number of the device or other identifier necessary to provide for effective tracking of the device;

- the date the device was shipped by the manufacturer

- the name, address, telephone number of the multiple distributor

- the name, address, telephone number, and social security number (if available) of the patient using the device.

- the location of the device

- the date the device was provided for use by the patient

- the name, address, and telephone number of the prescribing physician; and

- when applicable, the date the device was returned to the manufacturer, permanently retired from use, or otherwise permanently disposed of.

CURRENT RECORDS

- Manufacturers of tracked devices must keep current records in accordance with its SOPs for as long as the device is in use or distribution.

STANDARD OPERATING PROCEDURES

- Manufacturers of tracked device shall establish a written SOP for the collection, maintenance and auditing of the data specified for tracking in 821.25.

- Written SOPs shall incorporate the following:

    - Data collection and recording procedures including explanations of when and why required data could not be collected

    - Recording all modifications or changes to tracking system or the data collected/maintained, including dates and reasons for the modification/changes.

    - A quality assurance program that includes a statistically relevant audit at no less than 6 month intervals for the first three years of distribution and at least once a year thereafter.

NOTIFICATION

- When manufacturers of tracked devices become aware that a distributor, final distributor, or multiple distributor of the manufacturer's devices has failed to comply with their respective tracking obligations per 821.30, they are required to notify their local FDA District Office, per 821.25(d).

- When manufacturers of tracked devices permanently discontinues doing business, they are required to notify FDA at the time they notify any government agency, court, or supplier, and provide FDA with a complete set of its tracking records and information, per 821.1(e).

EXEMPTIONS & VARIANCES, 821.2

- If the firms indicates they have an exemption or variance from tracking verify/confirm that the document was issued by the OC, CDRH.

ATTACHMENT G

SUMMARY OF CORRECTIONS AND REMOVALS (CAR) REQUIREMENTS

21 CFR PART 806 REQUIREMENTS

1. Reports of Corrections and Removals - 806.10

Each device manufacturer and importer shall submit a written report to FDA of any correction or removal of a device IF the correction or removal was initiated to:

a) Reduce a risk to health posed by the device; or

b) Remedy a violation of the act caused by the device which may present a risk to health.

c) Reports in items (a) and (b) above are NOT required IF:

1. - The information has already been reported to FDA under the MDR regulation, 21 CFR Part 803 or under 21 CFR 1004.

2. - The correction or removal meets the following criteria:

- When the action is taken to improve the performance or quality of a device but does not reduce a risk to health posed by the device or remedy a violation of the act caused by the device

- Market withdrawals, 806.2(h) - a correction or removal of a distributed device that involves a minor violation of the act that would not be subject to legal action by FDA or that involves no violation of the act, e.g., normal stock rotation practices.

- Routine servicing, 806.2(k) - any regularly scheduled maintenance of a device, including the replacement of parts at the end of their normal life expectancy, e.g., calibration, replacement of batteries, and responses to normal wear and tear.

However, repairs of an unexpected nature, replacement of parts earlier than their normal life expectancy. or identical repairs or replacement of multiple units

of a device are not routine servicing.

- Stock recoveries, 806.2(l) - the correction or removal of a device that has not been marketed or that has not left the direct control of the manufacturer, i.e., the device is located on the premises owned, or under the control of, the manufacturer, and no portion of the lot, model, code, or other relevant unit involved in the corrective or removal action has been released for sale or use.

d) The key concept for determining when an event is reportable is the CAR regulation's definitions of risk to health:

1. A reasonable probability that use of, or exposure to, the product will cause serious adverse health consequences or death; (Class I Recalls) or

2. That use of, or exposure to, the product may cause temporary or medically reversible adverse health consequences, or an outcome where the probability of serious adverse health consequences is remote, (Class II Recall).

NOTE: Assistance regarding risk to health determinations can be obtained from your district's recall coordinator or CDRH's recall staff in the Office of Compliance.

e) Manufacturers and Distributors are required to submit a CAR report to the appropriate FDA District Office within 10 working days of initiating a correction. A list of the information required on the report is listed in 21 CFR 806.10(c)(1-13).

f) A foreign manufacturer or owner or operator of devices must also submit reports of corrections and removals.

NOTE: The regulation does not specify where foreign device manufacturers should send their CAR reports. FDA, however, expects foreign CAR reports to be submitted to the District Office where the product is being imported.

2. Records of corrections and removals not required to be reported, 806.20:

a) Each device manufacturer and distributor who initiates a correction or removal of a device that is NOT required to be

reported to FDA under Section 806.10 shall keep a record of each correction or removal.

b) Records of corrections and removals NOT reported to FDA must contain the following information:

(1) The brand name, common or usual name, classification, name, product code (if known), and the intended use of the device.

(2) The model, catalog, or code number of the device and the manufacturing lot or serial number of the device or other identification number.

(3) A description of the event(s) giving rise to the information reported and the corrective or removal action that has been, and is expected to be taken.

(4) Justification for NOT reporting the correction or removal action to FDA, which shall contain conclusions and any follow-ups, and be reviewed and evaluated by a designated person.

(5) A copy of all communications regarding the correction or removal.

c) Manufacturers shall retain all records required under this section for a period of 2 years beyond the expected life of the device, even if the respective firm has ceased to manufacturer or import the devices.

In addition, CAR files/records must be transferred to any new/subsequent manufacturer or importer of the device and maintained for the required period of time.

REPORTS OF CORRECTIONS AND REMOVALS REFERENCE MATERIAL

1. Title 21 CFR Part 806, Medical Devices; Reports of Corrections and Removals.

2. Medical Devices: Reports of Corrections and Removals Guidance. Issued by Lillian Gill, Director Office of Compliance/CDRH 9/17/97.

3. Title 21 CFR Part 7, Enforcement Policy, (Recalls (Including Product Corrections)---Guidelines on Policy, Procedures, and Industry Responsibilities.

4. Title 21 CFR Part 803, Medical Device User Facility and Manufacturer Reporting.